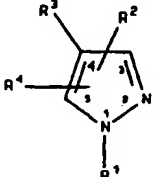




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

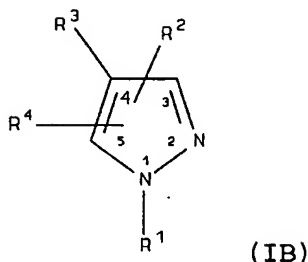
<p>(51) International Patent Classification <sup>7</sup> :</p> <p>C07D 401/04, A61K 31/415, 31/47, 31/445, 31/44, 31/50, 31/505, 31/52, C07D 405/14, 401/14, 409/14, 403/04, 487/04, 473/00, 413/14, 417/14, 471/04, A61P 29/00 // (C07D 487/04, 293:00, 231:00) (C07D 471/04, 221:00, 209:00)</p>	<p>A1</p>	<p>(11) International Publication Number: <b>WO 00/31063</b></p>
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<p>(54) Title: SUBSTITUTED PYRAZOLES AS p38 KINASE INHIBITORS</p>		
<div style="text-align: center;">  <p>(IA)</p> </div>		
<p>(57) Abstract</p> <p>A class of pyrazole derivatives is described for use in treating p38 kinase mediated disorders. Compounds of particular interest are defined by Formula (IA), wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> are as described in the specification.</p>		

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WHAT IS CLAIMED IS:

1. A compound of Formula IB:



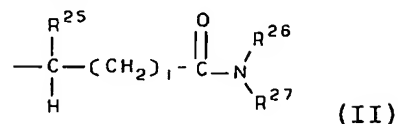
wherein

- 5         $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxy carbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocycliloxy carbonylalkylene, alkoxy carbonylaryl, aryloxy carbonylaryl, heterocycliloxy carbonylaryl, alkyl carbonylalkylene, aryl carbonylalkylene, heterocyclyl carbonylalkylene, alkyl carbonylaryl, aryl carbonylaryl, heterocyclyl carbonylaryl, alkyl carbonyloxyalkylene, aryl carbonyloxyalkylene, heterocyclyl carbonyloxyalkylene, alkyl carbonyloxyaryl, heterocyclyl carbonyloxyaryl,

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30 arylcarbonyloxyarylene, and  
heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



wherein:

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35      i is an integer from 0 to 9;
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R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and

40 heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxy-carbonylalkylene, alkoxy-carbonyl-heterocyclyl, alkoxy-carbonyl-heterocyclyl-carbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxy-carbonylarylene, aryloxy-carbonylarylene, alkylaryloxy-carbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxy-carbonyl-heterocyclylarylene,

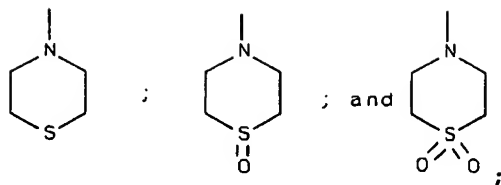
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alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or  
R<sup>27</sup> is -CHR<sup>28</sup>R<sup>29</sup> wherein R<sup>28</sup> is alkoxycarbonyl, and R<sup>29</sup>  
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or  
R<sup>26</sup> and R<sup>27</sup> together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

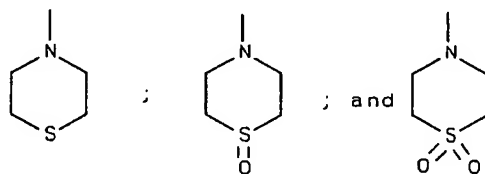


$R^2$  is piperidinyl substituted with one or more  
100 substituents selected from hydroxyalkyl, hydroxyalkenyl,  
hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene,  
alkoxyalkynylene, and hydroxyacyl, wherein said  
hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl,  
alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, and  
105 hydroxyacyl substitutents may be optionally substituted  
with one or more substituents selected from cycloalkyl,  
alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl,  
wherein said cycloalkyl, alkyl, aryl, arylalkyl,  
haloalkyl, and heteroarylalkyl substituents may be  
110 optionally substituted with one or more substituents  
selected from alkylene, alkynylene, hydroxy, halo,  
haloalkyl, alkoxy, keto, amino, nitro, cyano,  
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
aryloxy, heterocyclyl, and heteroaralkoxy; or  
115  $R^2$  is piperidinyl substituted with one or more  
substituents selected from hydroxycycloalkyl and  
alkoxycycloalkyl, and wherein said hydroxycycloalkyl and  
alkoxycycloalkyl substitutents may be optionally  
substituted with one or more substituents selected from  
120 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and  
heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl,  
arylalkyl, haloalkyl, and heteroarylalkyl substituents  
may be optionally substituted with one or more  
substituents selected from alkylene, alkynylene, hydroxy,  
125 halo, haloalkyl, alkoxy, keto, amino, nitro, cyano,  
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
aryloxy, heterocyclyl, and heteroaralkoxy; and  
 $R^3$  is selected from pyridinyl, pyrimidinyl,  
quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
130 thiazolylalkyl, thiazolylamino,

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wherein the R<sup>3</sup> pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 135 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more  
 substituents independently selected from hydrogen, aryl,  
 140 alkylamino, alkylthio, alkyloxy, aryloxy, arylamino,  
 arylthio, aralkoxy, wherein said aryl, alkylamino,  
 alkylthio, alkyloxy, aryloxy, arylamino, arylthio,  
 aralkoxy substituents may be optionally substituted with  
 one or more alkylene, alkenylene, hydroxy, halo,  
 145 haloalkyl, alkoxy, keto, amino, nitro, cyano,  
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
 aryloxy, heterocyclyl, and heteroaralkoxy; and

R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl,  
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 150 R<sup>4</sup> is optionally substituted with one or more substituents  
 independently selected from halo, haloalkyl, haloalkoxy,  
 alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl,  
 wherein said haloalkyl, haloalkoxy, alkoxy, cyano,  
 hydroxy, alkyl, alkenyl, and alkynyl substituents may be  
 155 optionally substituted with one or more alkylene,  
 alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,  
 keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,  
 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and  
 heteroaralkoxy; or

160 a pharmaceutically-acceptable salt or tautomer

thereof.

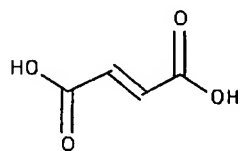
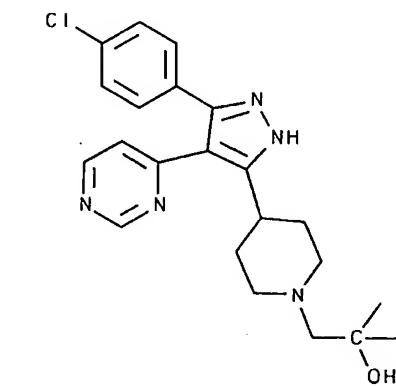
2. A compound of Claim 1 wherein:

$R^2$  is piperidinyl substituted with one or more substituents selected from hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl, wherein said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkylene, alkoxyalkenylene, alkoxyalkynylene, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

$R^2$  is piperidinyl substituted with one or more substituents selected from hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy.

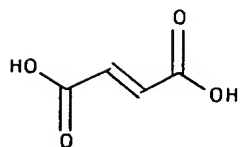
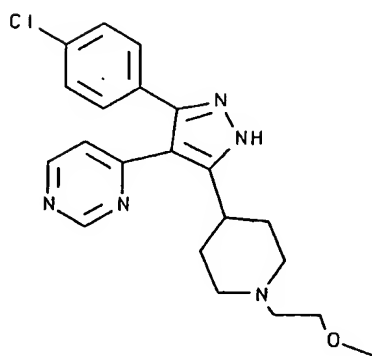
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3. A compound of Claim 1 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of:



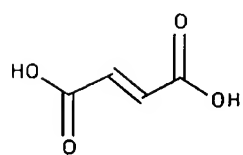
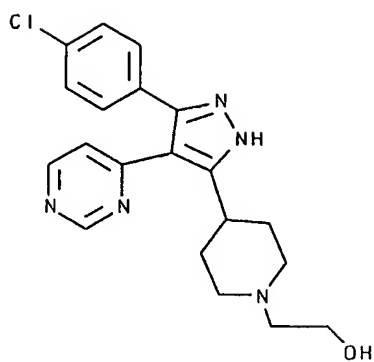
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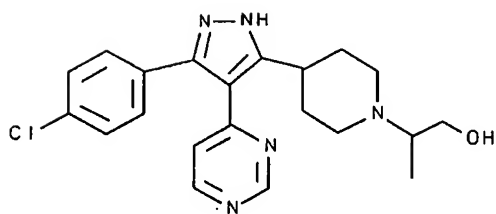


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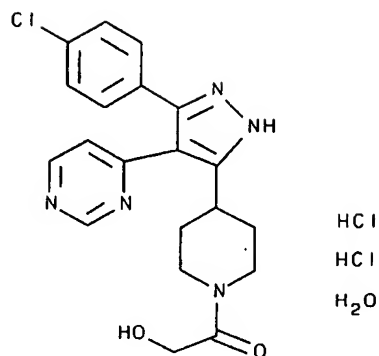


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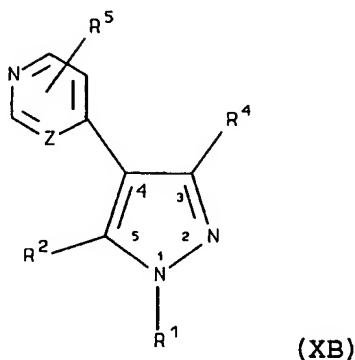


; and

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4. A compound of Claim 1 having Formula XB:



wherein

Z represents a carbon atom or a nitrogen atom;

R<sup>1</sup> is selected from hydrido, hydroxy, alkyl,  
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,  
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,  
 heterocyclylalkylene, haloalkyl, haloalkenyl,  
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,  
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,

alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,  
 heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl,  
 alkylthioalkylene, alkenylthioalkylene,  
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,  
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,  
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,  
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,  
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
 heterocyclylsulfonyl, alkylaminoalkylene,  
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,  
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,  
 heterocyclyloxycarbonylalkylene, alkoxycarbonylarylene,  
 aryloxycarbonylarylene, heterocyclyloxycarbonylarylene,  
 alkylcarbonylalkylene, arylcarbonylalkylene,  
 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 arylcarbonyloxyarylene, and  
 30 heterocyclylcarbonyloxyarylene; and

$R^2$  is piperidinyl substituted with one or more  
 substituents selected from hydroxyalkyl, hydroxyalkenyl,  
 alkoxyalkylene, alkoxyalkenylene, hydroxyalkylcarbonyl,  
 and hydroxyalkenylcarbonyl, wherein said hydroxyalkyl,  
 35 hydroxyalkenyl, alkoxyalkylene, alkoxyalkenylene,  
 hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl  
 substituents may be optionally substituted with one or  
 more substituents selected from cycloalkyl, alkyl, aryl,  
 arylalkyl, haloalkyl, and heteroarylalkyl, wherein said  
 40 cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and  
 heteroarylalkyl substituents may be optionally  
 substituted with one or more substituents selected from  
 alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy,  
 keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl,  
 45 alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and  
 heteroaralkoxy; or

R<sup>2</sup> is piperidinyl substituted with one or more substituents selected from hydroxycycloalkyl and hydroxycycloalkylcarbonyl, wherein said hydroxycycloalkyl and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents selected from cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R<sup>4</sup> is selected from cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R<sup>4</sup> is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

R<sup>5</sup> represents one or more substituents independently selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer



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thereof.

5. A compound of Claim 4 wherein R<sup>2</sup> is piperidinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine ring.

6. A compound of Claim 4 wherein Z represents a carbon atom.

7. A compound of Claim 4 wherein Z represents a nitrogen atom.

8. A compound of Claim 4 wherein R<sup>1</sup> is selected from hydrido, alkyl, hydroxyalkyl and alkynyl.

9. A compound of Claim 4 wherein R<sup>1</sup> is hydrido.

10. A compound of Claim 4 wherein R<sup>2</sup> is piperidinyl substituted with at least one substituent selected from lower hydroxyalkyl, lower hydroxyalkylcarbonyl and hydroxycycloalkylcarbonyl.

11. A compound of Claim 4 wherein R<sup>4</sup> is optionally substituted phenyl.

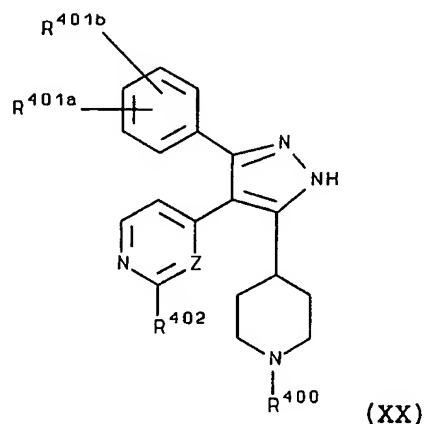
12. A compound of Claim 4 wherein R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

13. A compound of Claim 4 wherein R<sup>4</sup> is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

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14. A compound of Claim 4 wherein R<sup>5</sup> is hydrido.

15. A compound of Claim 1 having Formula XX:



wherein:

Z represents a carbon atom or a nitrogen atom;

5        R<sup>400</sup> is selected from hydroxyalkyl,  
hydroxyalkylcarbonyl and alkoxyalkylene, wherein said  
hydroxyalkyl, hydroxyalkylcarbonyl and alkoxyalkylene may  
be optionally substituted with one or more substituents  
selected from cycloalkyl, alkyl, aryl, arylalkyl,  
10        haloalkyl, and heteroarylalkyl, wherein said cycloalkyl,  
alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl  
substituents may be optionally substituted with one or  
more substituents selected from alkylene, alkynylene,  
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,  
15        cyano, alkylsulfonyl, alkylsulfinyl, alkylthio,  
alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy;  
or

      R<sup>400</sup> is hydroxycycloalkylcarbonyl that is optionally  
substituted with one or more substituents selected from  
20        cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and

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heteroarylalkyl, wherein said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from alkylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

$R^{401a}$  and  $R^{401b}$  are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

$R^{402}$  is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

a pharmaceutically-acceptable salt or tautomer thereof.

16. A compound of Claim 15 wherein:

$R^{400}$  is selected from lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene, wherein said lower hydroxyalkyl, lower hydroxyalkylcarbonyl and lower alkoxyalkylene may be optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and

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lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

R<sup>400</sup> is hydroxycycloalkylcarbonyl that is optionally substituted with one or more substituents selected from cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl, wherein said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl substituents may be optionally substituted with one or more substituents selected from lower alkylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, aryloxy, heterocyclyl, and lower heteroaralkoxy; and

R<sup>401a</sup> and R<sup>401b</sup> are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

R<sup>402</sup> is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said

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phenyl, lower alkylamino, lower alkylthio, lower  
alkyloxy, phenyloxy, phenylamino, phenylthio, and  
45 phenylalkoxy may be optionally substituted with one or  
more lower alkylene, lower alkenylene, hydroxy, halo,  
lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano,  
lower alkylsulfonyl, lower alkylsulfinyl, lower  
alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl,  
50 and lower heteroaralkoxy; or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

17. A compound of Claim 15 wherein Z represents a  
carbon atom.

18. A compound of Claim 15 wherein Z represents a  
nitrogen atom.

19. A compound of Claim 15 wherein R<sup>400</sup> is  
optionally substituted hydroxyalkylcarbonyl.

20. A compound of Claim 15 wherein R<sup>400</sup> is  
optionally substituted hydroxycycloalkylcarbonyl.

21. A compound of Claim 15 wherein R<sup>400</sup> is  
optionally substituted alkoxyalkylene.

22. A compound of Claim 15 wherein R<sup>400</sup> is  
optionally substituted hydroxyalkyl.

23. A compound of Claim 15 wherein R<sup>401</sup> represents  
one or more chloro, fluoro, bromo and iodo.

24. A compound of Claim 15 wherein R<sup>401</sup> is meta-  
chloro or para-chloro.

25. A compound of Claim 15 wherein R<sup>402</sup> is hydrido.

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26. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower  
hydroxyalkylcarbonyl;

R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

5 and

R<sup>402</sup> is hydrido.

27. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted 2-  
hydroxyacetyl, 2-hydroxy-propionyl, 2-hydroxy-2-  
methylpropionyl, 2-hydroxy-2-phenylacetyl, 3-  
5 hydroxypropionyl, 2-hydroxy-3-methylbutyryl, 2-  
hydroxyisocapropyl, 2-hydroxy-3-phenylpropionyl, and 2-  
hydroxy-3-imidazolylpropionyl;

R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

and

10 R<sup>402</sup> is hydrido.

28. A compound of Claim 27 wherein R<sup>401a</sup> is meta-  
chloro or para-chloro.

29. A compound of Claim 27 wherein R<sup>401a</sup> is para-  
chloro and R<sup>401b</sup> is hydrogen.

30. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower  
hydroxycycloalkylcarbonyl;

R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

5 and

R<sup>402</sup> is hydrido.

31. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted 1-  
hydroxy-1-cyclohexylacetyl, 2-hydroxy-1-cyclohexylacetyl,  
3-hydroxy-1-cyclohexylacetyl, 4-hydroxy-1-  
5 cyclohexylacetyl, 1-hydroxy-1-cyclopentylacetyl, 2-

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hydroxy-1-cyclopentylacetyl, and 3-hydroxy-1-cyclopentylacetyl, 2-hydroxy-2-cyclohexylacetyl;

R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;  
and

10 R<sup>402</sup> is hydrido.

32. A compound of Claim 31 wherein R<sup>401a</sup> is meta-chloro or para-chloro.

33. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower hydroxyalkyl;

R<sup>401</sup> is selected from chloro, fluoro, bromo and iodo;

and

5 R<sup>402</sup> is hydrido.

34. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxyisopropyl;

5 R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;  
and

R<sup>402</sup> is hydrido.

35. A compound of Claim 34 wherein R<sup>401a</sup> is meta-chloro or para-chloro.

36. A compound of Claim 15 wherein:

R<sup>400</sup> is optionally substituted lower alkoxyalkylene;

R<sup>401a</sup> is selected from chloro, fluoro, bromo and iodo;

and

5 R<sup>402</sup> is hydrido.

37. A compound of Claim 15 wherein:

R<sup>400</sup> is selected from optionally substituted methoxymethylene, methoxyethylene, methoxypropylene, methoxyisopropylene, ethoxymethylene, ethoxyethylene,

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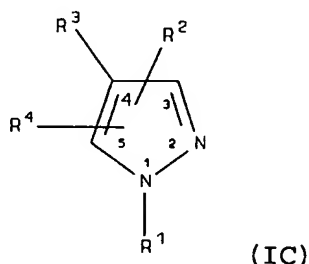
5 ethoxypropylene, and ethoxyisopropylene.

$R^{401a}$  is selected from chloro, fluoro, bromo and iodo;  
and

$R^{402}$  is hydrido.

38. A compound of Claim 37 wherein  $R^{401a}$  is meta-chloro or para-chloro.

39. A compound of Formula IC:



5 wherein

$R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxy carbonylalkylene, aryloxycarbonylalkylene,

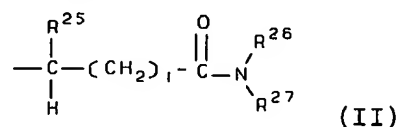
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heterocyclyloxy carbonylalkylene, alkoxycarbonylarylene,  
 25 aryloxy carbonylarylene, heterocyclyloxy carbonylarylene,  
 alkylcarbonylalkylene, arylcarbonylalkylene,  
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 30 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



35 wherein:

i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 40 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxycarbonylalkylene, and alkylaminoalkyl; and

45 R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 50 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
 aryloxyarylene, aralkoxyarylene,  
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
 55 alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,  
 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,

alkylaminoalkylene, arylaminocarbonylalkylene,  
alkoxyarylaminoalkylene, aminocarbonylalkylene,  
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,  
60 arylcarbonylalkylene, alkoxycarbonylarylene,  
aryloxyalkylene, alkylaryloxyalkylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxyalkylene,  
65 heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
70 said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyalkylene, aryloxyalkylene, arylaminocarbonylalkylene,  
aryloxyalkylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
75 arylthioalkylarylene, and alkylsulfonylarylene groups  
may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
80 is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
85 one or more radicals independently selected from alkyl  
and nitro; or

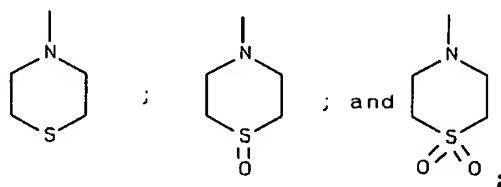
$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
90 radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,

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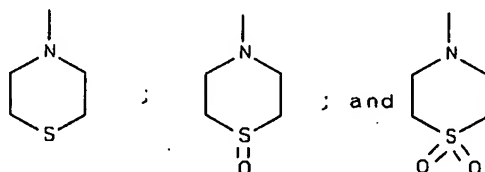
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
 alkoxy carbonyl, aralkoxy carbonyl, alkylamino and  
 95 alkoxy carbonylamino; wherein said aryl,  
 heterocyclalkylene and aryloxyalkylene radicals may be  
 optionally substituted with one or more radicals  
 independently selected from halogen, alkyl and alkoxy;  
 and

100 R<sup>2</sup> is cyclohexyl substituted with one or more  
 substituents selected from optionally substituted  
 hydroxyalkyl, alkylaminoalkylene and cycloalkylamino; and

R<sup>3</sup> is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 105 thiazolylalkyl, thiazolylamino,



wherein the R<sup>3</sup> pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 110 thiazolylalkyl, thiazolylamino,

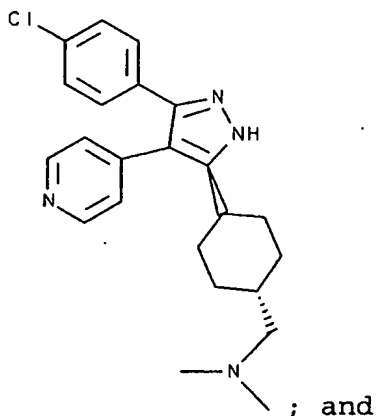


groups may be optionally substituted with one or more  
 substituents independently selected from hydrogen, aryl,  
 115 alkylamino, alkylthio, alkyloxy, aryloxy, arylamino,  
 arylthio, aralkoxy, wherein said aryl, alkylamino,  
 alkylthio, alkyloxy, aryloxy, arylamino, arylthio,  
 aralkoxy substituents may be optionally substituted with  
 one or more alkylene, alkenylene, hydroxy, halo,  
 120 haloalkyl, alkoxy, keto, amino, nitro, cyano,  
 alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
 aryloxy, heterocyclyl, and heteroaralkoxy; and

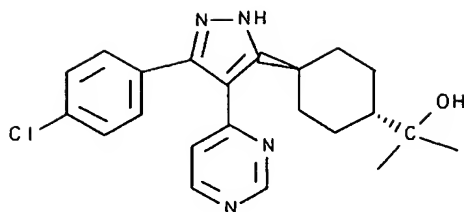
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R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
125 R<sup>4</sup> is optionally substituted with one or more substituents independently selected from halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl substituents may be  
130 optionally substituted with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or  
135 a pharmaceutically-acceptable salt or tautomer thereof.

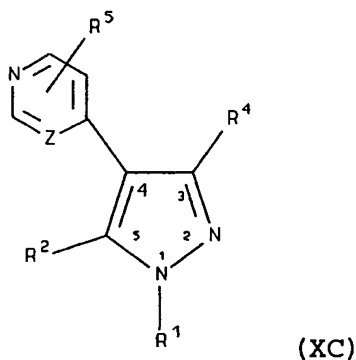
40. A compound of Claim 39 selected from compounds, their tautomers and their pharmaceutically acceptable salts, of the group consisting of :



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41. A compound of Claim 39 having Formula XC:



wherein

Z represents a carbon atom or a nitrogen atom;

- R<sup>1</sup> is selected from hydrido, hydroxy, alkyl,  
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,  
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,  
 heterocyclylalkylene, haloalkyl, haloalkenyl,  
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,  
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,  
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,  
 heterocyclloxyalkyl, alkoxyalkoxy, mercaptoalkyl,  
 alkylthioalkylene, alkenylthioalkylene,  
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,  
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,

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- alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,  
arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,  
alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
heterocyclylsulfonyl, alkylaminoalkylene,  
20 alkylsulfonylalkylene, acyl, acyloxy carbonyl,  
alkoxycarbonylalkylene, aryloxy carbonylalkylene,  
heterocycliloxy carbonylalkylene, alkoxycarbonylarylene,  
aryloxy carbonylarylene, heterocycliloxy carbonylarylene,  
alkylcarbonylalkylene, arylcarbonylalkylene,  
25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
arylcarbonylarylene, heterocyclylcarbonylarylene,  
alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
arylcarbonyloxyarylene, and  
30 heterocyclylcarbonyloxyarylene; and  
R<sup>2</sup> is cyclohexyl substituted with one or more  
substituents selected from optionally substituted  
hydroxyalkyl, alkylaminoalkylene and cycloalkylamino; and  
R<sup>4</sup> is selected from cycloalkyl, cycloalkenyl, aryl,  
35 and heterocyclyl, wherein R<sup>4</sup> is optionally substituted  
with one or more substituents independently selected from  
halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy,  
alkyl, alkenyl, and alkynyl, wherein said haloalkyl,  
haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl  
40 substituents may be optionally substituted with one or  
more alkylene, alkenylene, alkynylene, hydroxy, halo,  
haloalkyl, alkoxy, keto, amino, nitro, cyano,  
alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl,  
aryloxy, heterocyclyl, and heteroaralkoxy; and  
45 R<sup>5</sup> represents one or more substituents independently  
selected from hydrogen, aryl, alkylamino, alkylthio,  
alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein  
said aryl, alkylamino, alkylthio, alkyloxy, aryloxy,  
arylamino, arylthio, aralkoxy substituents may be  
50 optionally substituted with one or more alkylene,  
alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto,

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amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or

55       a pharmaceutically-acceptable salt or tautomer thereof.

42. A compound of Claim 41 wherein R<sup>2</sup> is cyclohexyl substituted with at least one substituent attached to the 4-position carbon ring atom of the cyclohexyl ring.

43. A compound of Claim 41 wherein Z represents a carbon atom.

44. A compound of Claim 41 wherein Z represents a nitrogen atom.

45. A compound of Claim 41 wherein R<sup>1</sup> is selected from hydrido, alkyl, hydroxyalkyl and alkynyl.

46. A compound of Claim 41 wherein R<sup>1</sup> is hydrido.

47. A compound of Claim 41 wherein R<sup>2</sup> is cyclohexyl substituted with one or more substituents selected from optionally substituted lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino.

48. A compound of Claim 41 wherein R<sup>4</sup> is optionally substituted phenyl.

49. A compound of Claim 41 wherein R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

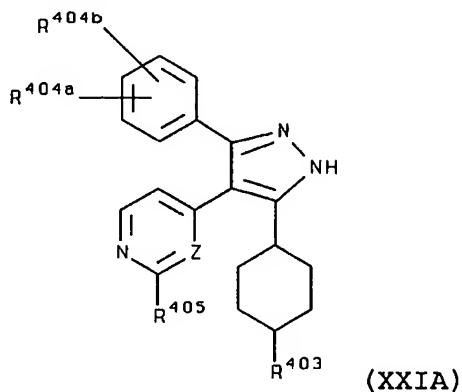
50. A compound of Claim 41 wherein R<sup>4</sup> is phenyl optionally substituted at the meta or para position with

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one or more chloro radicals.

51. A compound of Claim 41 wherein R<sup>5</sup> is hydrido.

52. A compound of Claim 41 having Formula XXIA:



wherein:

Z represents a carbon atom or a nitrogen atom;

R<sup>403</sup> is selected from hydroxyalkyl,

5 alkylaminoalkylene and cycloalkylamino; and

R<sup>404a</sup> and R<sup>404b</sup> are independently selected from  
hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano,  
hydroxy, alkyl, alkenyl, and alkynyl, wherein said  
haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl,  
10 and alkynyl substituents may be optionally substituted  
with one or more alkylene, alkenylene, alkynylene,  
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,  
cyano, alkylsulfonyl, alkylsulfinyl, alkylthio,  
alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy;  
15 and

R<sup>405</sup> is selected from hydrogen, aryl, alkylamino,  
alkylthio, alkyloxy, aryloxy, arylamino, arylthio,  
aralkoxy, wherein said aryl, alkylamino, alkylthio,  
alkyloxy, aryloxy, arylamino, arylthio, aralkoxy



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- 20 substituents may be optionally substituted with one or more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or
- 25 a pharmaceutically-acceptable salt or tautomer thereof.

53. A compound of Claim 52 wherein:

- $R^{403}$  is selected from lower hydroxyalkyl, lower alkylaminoalkylene and cycloalkylamino; and
- $R^{404a}$  and  $R^{404b}$  are independently selected from
- 5 alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene,
- 10 lower alkenylene, lower alkynylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and
- 15  $R^{405}$  is selected from hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and
- 20 phenylalkoxy may be optionally substituted with one or more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl,
- 25 and lower heteroaralkoxy; or
- a pharmaceutically-acceptable salt or tautomer thereof.

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54. A compound of Claim 52 wherein Z represents a carbon atom.

55. A compound of Claim 52 wherein Z represents a nitrogen atom.

56. A compound of Claim 52 wherein R<sup>403</sup> is optionally substituted hydroxyalkyl.

57. A compound of Claim 52 wherein R<sup>403</sup> is optionally substituted alkylaminoalkylene.

58. A compound of Claim 57 wherein R<sup>403</sup> is optionally substituted dialkylaminoalkylene.

59. A compound of Claim 52 wherein R<sup>403</sup> is optionally substituted cycloalkylamino.

60. A compound of Claim 52 wherein R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo.

61. A compound of Claim 52 wherein R<sup>404a</sup> is meta-chloro or para-chloro.

62. A compound of Claim 52 wherein R<sup>405</sup> is hydrido.

63. A compound of Claim 52 wherein:

R<sup>403</sup> is optionally substituted lower hydroxyalkyl;

R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;

5 and

R<sup>405</sup> is hydrido.

64. A compound of Claim 52 wherein:

R<sup>403</sup> is selected from optionally substituted hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxybutyl;

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5        R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;  
and

      R<sup>405</sup> is hydrido.

65. A compound of Claim 64 wherein R<sup>404a</sup> is meta-chloro or para-chloro.

66. A compound of Claim 52 wherein:

      R<sup>403</sup> is optionally substituted lower  
alkylaminoalkylene;

5        R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;  
and

      R<sup>405</sup> is hydrido.

67. A compound of Claim 52 wherein:

      R<sup>403</sup> is selected from optionally substituted  
methylaminomethylene, methylaminoethylene,  
methylaminopropylene, ethylaminomethylene,  
5        ethylaminoethylene, ethylaminopropylene,  
propylaminomethylene, propylaminoethylene,  
propylaminopropylene, dimethylaminomethylene,  
dimethylaminoethylene, dimethylaminopropylene,  
diethylaminomethylene, diethylaminoethylene,  
10        diethylaminopropylene, dipropylaminomethylene,  
dipropylaminoethylene, and dipropylaminopropylene;

      R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;  
and

      R<sup>405</sup> is hydrido.

68. A compound of Claim 67 wherein R<sup>404a</sup> is meta-chloro or para-chloro.

69. A compound of Claim 52 wherein:

      R<sup>403</sup> is optionally substituted cycloalkylamino;

      R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;  
and

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5         $R^{405}$  is hydrido.

70. A compound of Claim 52 wherein:

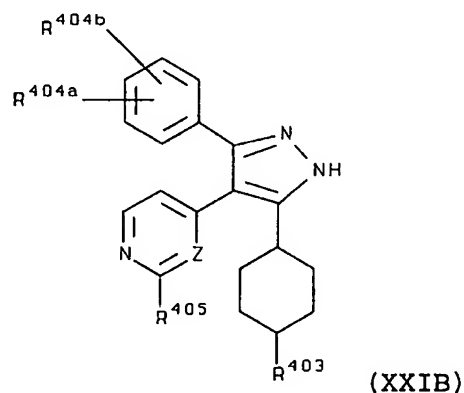
$R^{403}$  is selected from optionally substituted  
cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl;

$R^{404a}$  is selected from chloro, fluoro, bromo and iodo;

5        and

$R^{405}$  is hydrido.

71. A compound of Formula XXIB:



wherein:

Z represents a carbon atom or a nitrogen atom;

$R^{403}$  is selected from alkylamino; and

5         $R^{404a}$  and  $R^{404b}$  are independently selected from  
hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano,  
hydroxy, alkyl, alkenyl, and alkynyl, wherein said  
haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl,  
and alkynyl substituents may be optionally substituted  
10        with one or more alkylene, alkenylene, alkynylene,  
hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro,

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cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

- 15         $R^{405}$  is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or  
20 more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or  
      a pharmaceutically-acceptable salt or tautomer  
25 thereof.

72. A compound of Claim 71 wherein:

$R^{403}$  is selected from lower alkylamino; and

- $R^{404a}$  and  $R^{404b}$  are independently selected from hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and  
5 lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower  
10 haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and

- $R^{405}$  is selected from hydrogen, phenyl, lower  
15 alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or  
20 more lower alkylene, lower alkenylene, hydroxy, halo,

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lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or

25       a pharmaceutically-acceptable salt or tautomer thereof.

73. A compound of Claim 71 wherein Z represents a carbon atom.

74. A compound of Claim 71 wherein Z represents a nitrogen atom.

75. A compound of Claim 71 wherein R<sup>403</sup> is optionally substituted dialkylamino.

76. A compound of Claim 71 wherein R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo.

77. A compound of Claim 71 wherein R<sup>404a</sup> is meta-chloro or para-chloro.

78. A compound of Claim 71 wherein R<sup>405</sup> is hydrido.

79. A compound of Claim 71 wherein:

R<sup>403</sup> is optionally substituted lower alkylamino;

R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;

and

5       R<sup>405</sup> is hydrido.

80. A compound of Claim 71 wherein:

R<sup>403</sup> is selected from optionally substituted methylamino, ethylamino, n-propylamino, isopropylamino, n-butylamino, sec-butylamino, t-butylamino, isobutylamino, dimethylamino, diethylamino, di-n-propylamino, di-isopropylamino, di-n-butylamino, di-sec-

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butylamino, di-t-butylamino, and di-isobutylamino;

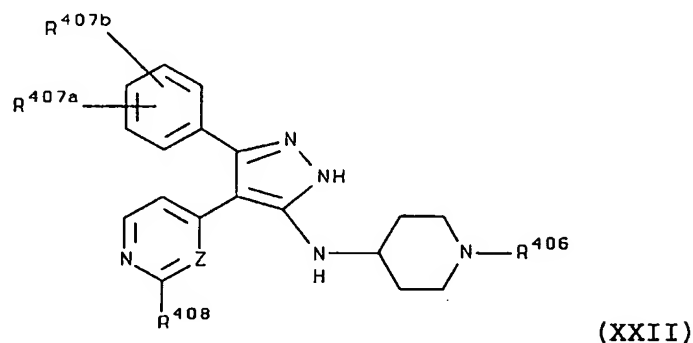
R<sup>404a</sup> is selected from chloro, fluoro, bromo and iodo;

and

10 R<sup>405</sup> is hydrido.

81. A compound of Claim 80 wherein R<sup>404a</sup> is meta-chloro or para-chloro.

82. A compound Formula XXII:



wherein:

Z represents a carbon atom or a nitrogen atom;

R<sup>406</sup> is alkynyl; and

5 R<sup>407a</sup> and R<sup>407b</sup> are independently selected from hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl substituents may be optionally substituted

10 with one or more alkylene, alkenylene, alkynylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; and

15 R<sup>408</sup> is selected from hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio,

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aralkoxy, wherein said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, aralkoxy substituents may be optionally substituted with one or  
20 more alkylene, alkenylene, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroaralkoxy; or  
a pharmaceutically-acceptable salt or tautomer  
25 thereof.

83. A compound of Claim 82 wherein:  
R<sup>406</sup> is selected from lower alkynyl; and  
R<sup>407a</sup> and R<sup>407b</sup> are independently selected from  
hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower  
alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and  
5 lower alkynyl, wherein said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl substituents may be optionally substituted with one or more lower alkylene, lower alkenylene, lower alkynylene, hydroxy, halo, lower  
10 haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; and  
R<sup>408</sup> is selected from hydrogen, phenyl, lower  
15 alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or  
20 more lower alkylene, lower alkenylene, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroaralkoxy; or  
25 a pharmaceutically-acceptable salt or tautomer



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thereof.

84. A compound of Claim 82 wherein Z represents a carbon atom.

85. A compound of Claim 82 wherein Z represents a nitrogen atom.

86. A compound of Claim 82 wherein  $R^{407a}$  is selected from chloro, fluoro, bromo and iodo.

87. A compound of Claim 82 wherein  $R^{407a}$  is meta-chloro or para-chloro.

88. A compound of Claim 82 wherein  $R^{408}$  is hydrido.

89. A compound of Claim 82 wherein:

$R^{406}$  is optionally substituted lower alkynyl;

$R^{407a}$  is selected from chloro, fluoro, bromo and iodo;

and

5  $R^{408}$  is hydrido.

90. A compound of Claim 82 wherein:

$R^{406}$  is selected from optionally substituted ethynyl, propynyl and butynyl;

$R^{407a}$  is selected from chloro, fluoro, bromo and iodo;

5 and

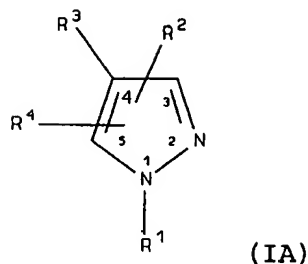
$R^{408}$  is hydrido.

91. A compound of Claim 82 wherein  $R^{406}$  is propargyl.

92. A compound of Claim 82 wherein  $R^{407a}$  is meta-chloro or para-chloro.

93. A compound of Formula IA

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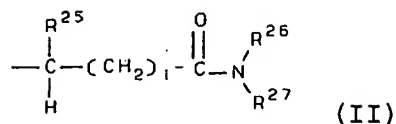


wherein

- R<sup>1</sup> is selected from hydrido, hydroxy, alkyl,  
 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl,  
 heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene,  
 heterocyclalkylene, haloalkyl, haloalkenyl,  
 haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,  
 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl,  
 alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,  
 heterocyclloxyalkyl, alkoxyalkoxy, mercaptoalkyl,  
 alkylthioalkylene, alkenylthioalkylene,  
 alkylthioalkenylene, amino, aminoalkyl, alkylamino,  
 15 alkenylamino, alkynylamino, arylamino, heterocyclylamino,  
 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,  
 arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl,  
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
 heterocyclylsulfonyl, alkylaminoalkylene,  
 20 alkylsulfonylalkylene, acyl, acyloxycarbonyl,  
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,  
 heterocyclloxy carbonylalkylene, alkoxycarbonylarylene,  
 aryloxycarbonylarylene, heterocyclloxy carbonylarylene,  
 alkylcarbonylalkylene, arylcarbonylalkylene,  
 25 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 arylcarbonyloxyarylene, and  
 30 heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula

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wherein:

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i is an integer from 0 to 9;
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35 R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclalkylcarbonylaminoalkylene; and

40 R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxy carbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocyclyl, alkylheterocyclylalkylene, alkylheterocyclylarylene, aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclylalkylene, aryloxyalkoxyarylene, alkoxy-carbonylalkylene, alkoxy-carbonyl-heterocyclyl, alkoxy-carbonyl-heterocyclyl-carbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxy-carbonylarylene, aryloxy-carbonylarylene, alkylaryloxy-carbonylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxy-carbonyl-heterocyclylarylene, alkoxy-carbonylalkoxylarylene, heterocyclylcarbonylalkylarylene, alkylthioalkylene, cycloalkylthioalkylene, alkylthioarylene,

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65 aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, and alkylaminosulfonylarylene;  
wherein said alkyl, cycloalkyl, aryl, heterocyclyl,  
aralkyl, heterocyclylalkylene, alkylheterocyclylarylene,  
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
may be optionally substituted with one or more radicals  
75 independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
80 alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
and nitro; or

85  $R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
90 alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
heterocyclylalkylene and aryloxyalkylene radicals may be  
95 optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is selected from mercapto,  
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,  
100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,

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aminoalkylcarbonylaminoalkylene,  
 alkylaminoalkylcarbonylamino, aminoalkylthio,  
 alkylaminocarbonylalkylthio,  
 alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,  
 105 alkenylthio, alkynylthio, carboxyalkylthio,  
 alkoxyalkylthio, alkylsulfinyl, alkylsulfonyl,  
 alkoxyalkyl, alkoxyalkylthio, alkoxyalkylamino,  
 alkoxyalkylaminoalkylene, alkoxyalkylaminoalkoxy,  
 aralkylthio, heterocyclalkylthio, aminoalkoxy,  
 110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 alkenyloxy, alkynyloxy, and heterocyclalkyloxy; or

$R^2$  is  $R^{200}$ -heterocyclalkyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 cycloalkyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

- 115 -  $(CR^{202}R^{203})_y-$ ;  
 -  $C(O)-$ ;  
 -  $C(O)-(CH_2)_y-$ ;  
 -  $C(O)-O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-C(O)-$ ;  
 120 -  $O-(CH_2)_y-C(O)-$ ;  
 -  $NR^{202}-$ ;  
 -  $NR^{202}-(CH_2)_y-$ ;  
 -  $(CH_2)_y-NR^{202}-$ ;  
 -  $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;  
 125 -  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-$ ;  
 -  $(CR^{202}R^{203})_y-S(O)_x-$ ;  
 130 -  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;  
 -  $O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-O-$ ;  
 -  $S-$ ; and  
 135 -  $O-$ ;  
 or  $R^{200}$  represents a bond;

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$R^{201}$  represents one or more radicals selected from the group consisting of hydroxy, hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkylene, alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkylene, aminoalkyl, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido, alkyl, aryl and aralkyl; and

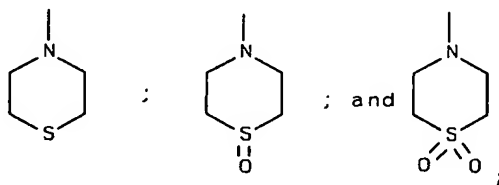
y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

$R^2$  is  $-NHCR^{204}R^{205}$  wherein  $R^{204}$  is alkylaminoalkylene, and  $R^{205}$  is aryl; or

$R^2$  is  $-C(NR^{206})R^{207}$  wherein  $R^{206}$  is selected from hydrogen and hydroxy, and  $R^{207}$  is selected from alkyl, aryl and aralkyl; and

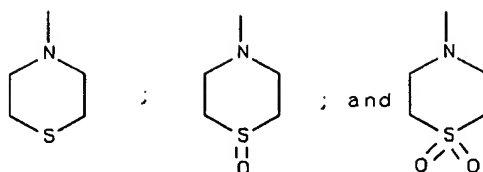
$R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



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wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

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groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxy carbonyl, heterocyclyl oxycarbonyl, alkoxycarbonylamino, alkoxyaryl amino, alkoxyaralkyl amino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonyl heterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and

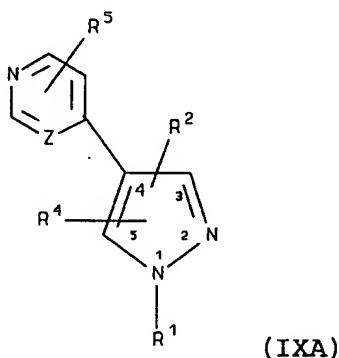
$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  $R^4$  is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

200

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- alkylsulfinylalkylene, arylsulfinylalkylene,  
 alkylsulfonyl, alkylsulfonylalkylene,  
 205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
 nitro, alkylamino, arylamino, alkylaminoalkylene,  
 arylaminoalkylene, aminoalkylamino, and hydroxy;  
 210 provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl  
 ring containing a 2-hydroxy substituent and when  $R^1$  is  
 hydrido; and  
 further provided  $R^2$  is selected from  $-R^{200}-$   
 heterocyclyl- $R^{201}$ ,  $-R^{200}-$ aryl- $R^{201}$ , or  $-R^{200}-$ unsubstituted  
 215 cycloalkyl- $R^{201}$  when  $R^4$  is hydrido; and  
 further provided that  $R^4$  is not methylsulfonylphenyl  
 or aminosulfonylphenyl; and  
 further provided that  $R^1$  is not methylsulfonylphenyl;  
 or  
 220 a pharmaceutically-acceptable salt or tautomer  
 thereof.

94. A compound of Formula IXA:



wherein

Z represents a carbon atom or a nitrogen atom; and

5  $R^1$  is selected from hydrido, lower alkyl, lower



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hydroxyalkyl, lower alkynyl, lower aralkyl, lower aminoalkyl and lower alkylaminoalkyl; and

$R^2$  is lower hydroxyalkylamino; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$  or  $R^{200}$ -cycloalkyl- $R^{201}$

10 wherein:

$R^{200}$  is selected from:

-  $(CR^{202}R^{203})_y-$ ;

-  $NR^{202}-$ ;

-  $NR^{202}-(CH_2)_y-$ ;

15 -  $(CH_2)_y-NR^{202}-$ ;

-  $O-(CH_2)_y-$ ;

-  $(CH_2)_y-O-$ ;

-  $S-$ ;

-  $O-$ ;

20 or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from the group consisting of hydroxy, lower hydroxyalkyl, lower cycloalkyl; lower hydroxyalkylcarbonyl, lower cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, lower alkoxyalkylene, lower alkoxyarylene, lower carboxyalkylcarbonyl, lower alkoxyalkylcarbonyl, lower heterocyclylalkylcarbonyl, lower alkylsulfonylalkylene, amino, lower aminoalkyl, lower aralkylamino, lower alkylaminoalkylene, aminocarbonyl, lower alkylcarbonylamino, lower alkylcarbonylaminoalkylene, lower alkylaminoalkylcarbonyl, lower alkylaminoalkylcarbonylamino, lower aminoalkylcarbonylaminoalkyl, lower alkoxycarbonylamino, lower alkoxyalkylcarbonylamino, lower alkoxycarbonylaminoalkylene, lower alkylimidocarbonyl, amidino, lower alkylamidino, lower aralkylamidino, guanidino, lower guanidinoalkylene, and lower alkylsulfonylamino; and

35  $R^{202}$  and  $R^{203}$  are independently selected from hydrido, lower alkyl, aryl and lower aralkyl; and

40  $y$  is 0, 1, 2 or 3; and

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R<sup>4</sup> is selected from aryl selected from phenyl, biphenyl, naphthyl, wherein said aryl is optionally substituted at a substitutable position with one or more radicals independently selected from halo, lower alkyl, lower alkoxy, aryloxy, lower aralkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, and hydroxy; and

R<sup>5</sup> is selected from hydrido, halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower aralkyl, lower aralkyloxy, lower aralkylamino, lower alkoxycarbonyl, lower alkylamino, lower hydroxyalkylamino, lower alkylcarbonyl, lower aralkenyl, lower arylheterocyclyl, carboxy, lower cycloalkylamino, lower hydroxycycloalkylamino, lower alkoxycarbonylamino, lower alkoxyaralkylamino, lower alkylaminoalkylamino, lower heterocyclylamino, lower heterocyclylalkylamino, lower aralkylheterocyclylamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyaralkylamino, hydrazinyl, and lower alkylhydrazinyl, or -NR<sup>62</sup>R<sup>63</sup> wherein R<sup>62</sup> is lower alkylcarbonyl or amino, and R<sup>63</sup> is lower alkyl or lower phenylalkyl; or

a pharmaceutically-acceptable salt or tautomer thereof.

95. A compound of Claim 94 wherein R<sup>2</sup> is R<sup>200</sup>-heterocyclyl-R<sup>201</sup>.

96. A compound of Claim 94 wherein R<sup>2</sup> is R<sup>200</sup>-cycloalkyl-R<sup>201</sup>.

97. A compound of Claim 94 wherein:

R<sup>1</sup> is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-piperidinyl-R<sup>201</sup>, R<sup>200</sup>-piperazinyl-R<sup>201</sup>, or R<sup>200</sup>-cyclohexyl-R<sup>201</sup> wherein:

R<sup>200</sup> is selected from:

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- (CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

-NR<sup>202</sup>-;

-S-;

10 -O-;

or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-  
15 1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene, propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,  
20 cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl,  
25 carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl,  
30 methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino,  
35 methylaminomethylene, ethylaminomethylene, methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminoethylene,  
40 ethylcarbonylaminoethylene, aminomethylcarbonylaminoethylmethylene, methoxycarbonylamino, ethoxycarbonylamino,

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methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
45 methoxycarbonylaminomethylene,  
ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
50 methylsulfonylamino; and  
R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
y is 0, 1 or 2; and  
R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
55 substituted with one or more radicals independently  
selected from methylthio, fluoro, chloro, bromo, iodo,  
methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy,  
trifluoromethyl, nitro, dimethylamino, and hydroxy; and  
R<sup>5</sup> is selected from hydrido, fluoro, chloro, bromo,  
60 iodo, hydroxy, methyl, ethyl, propyl, benzyl,  
fluorophenylethyl, fluorophenylethenyl,  
fluorophenylpyrazolyl, cyano, carboxy, methoxy,  
methoxycarbonyl, aminocarbonyl, acetyl, methylamino,  
dimethylamino, 2-methylbutylamino, ethylamino,  
65 dimethylaminoethylamino, hydroxyethylamino,  
hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
70 hydroxy)ethylamino, piperidinylamino,  
pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
75 fluorophenylethylamino, methylaminoethylamino,  
dimethylaminoethylamino, methylaminopropylamino,  
dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,

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80 dimethylaminopentylamino, ethylaminoethylamino,  
 diethylaminoethylamino, ethylaminopropylamino,  
 diethylaminopropylamino, ethylaminobutylamino,  
 diethylaminobutylamino, ethylaminopentylamino,  
 methylaminocarbonyl, methylcarbonyl, ethylcarbonyl,  
 hydrazinyl, and 1-methylhydrazinyl, or  $-NR^{62}R^{63}$  wherein  $R^{62}$   
 85 is methylcarbonyl or amino, and  $R^{63}$  is methyl or benzyl;  
 or

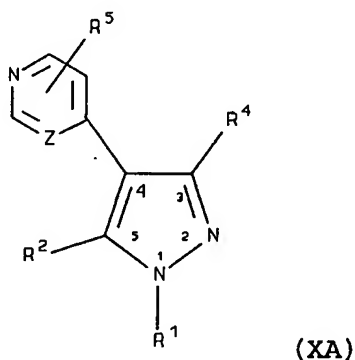
a pharmaceutically-acceptable salt or tautomer thereof.

98. A compound of Claim 97 wherein  $R^2$  is  $R^{200}$ -piperidinyl- $R^{201}$ .

99. A compound of Claim 97 wherein  $R^2$  is  $R^{200}$ -pyrazinyl- $R^{201}$ .

100. A compound of Claim 97 wherein  $R^2$  is  $R^{200}$ -cyclohexyl- $R^{201}$ .

101. A compound of Claim 94 having the Formula XA:



wherein:

$Z$  represents a carbon atom or a nitrogen atom; and  
 5  $R^1$  is selected from hydrido, methyl, ethyl,

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hydroxyethyl and propargyl; and

$R^2$  is  $R^{200}$ -piperidinyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

$-(CR^{202}R^{203})_y-$ ;

10  $-NR^{202}-$ ;

$-S-$ ;

$-O-$ ;

or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from

15 the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene,  
20 propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,  
25 hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
30 ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl,  
35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N,N-dipropylamino, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene,  
40 methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino,

- methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
45 aminomethylcarbonylaminocarbonylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene,  
50 ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
methylsulfonylamino; and  
55  $R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
y is 0, 1 or 2; and  
 $R^4$  is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
60 selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and  
 $R^5$  is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,  
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,  
65 methylamino, dimethylamino, 2-methylbutylamino,  
ethylamino, dimethylaminoethylamino, hydroxyethylamino,  
hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
70 imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
hydroxy)ethylamino, piperidinylamino,  
pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
75 phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminoethylamino,  
dimethylaminoethylamino, methylaminopropylamino,

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dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,  
80 dimethylaminopentylamino, ethylaminoethylamino,  
diethylaminoethylamino, ethylaminopropylamino,  
diethylaminopropylamino, ethylaminobutylamino,  
diethylaminobutylamino, ethylaminopentylamino,  
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;

85 or

a pharmaceutically-acceptable salt or tautomer thereof.

102. A compound of Claim 101 wherein:

R<sup>1</sup> is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-piperidinyl-R<sup>201</sup> wherein:

5 R<sup>200</sup> is selected from:

methylene;

-NR<sup>202</sup>-;

-S-;

-O-;

10 or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-  
dimethyl)ethyl, methoxymethyl, methoxyethyl,  
15 methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,  
propoxypropyl, methoxyphenyl, ethoxyphenyl,  
propoxyphenyl, hydroxymethylcarbonyl,  
hydroxyethylcarbonyl, carboxymethylcarbonyl,  
carboxyethylcarbonyl, methoxymethylcarbonyl,  
20 methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
25 propoxyphenylcarbonyl, methylsulfonylmethylene, amino,



aminomethyl, aminoethyl, aminopropyl, N-benzylamino, methylaminomethylene, aminocarbonyl, methoxycarbonylamino, ethoxycarbonylamino, or methylsulfonylamino; and

30         $R^{202}$  is selected from hydrido, methyl, ethyl, phenyl and benzyl; and

$R^4$  is phenyl, wherein said phenyl is optionally substituted with one or more radicals independently selected from fluoro, chloro, methyl, ethyl, methoxy and  
35        ethoxy; and

$R^5$  is selected from hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, ethylamino, dimethylaminoethylamino,  
40        hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino,  
45        methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino,  
50        methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl,  
55        methylcarbonyl, and ethylcarbonyl; or

      a pharmaceutically-acceptable salt or tautomer thereof.

103. A compound of Claim 101 wherein:

$R^1$  is hydrido; and

$R^2$  is  $R^{200}$ -piperidinyl- $R^{201}$  wherein:

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R<sup>200</sup> is selected from:

- 5       methylene;  
       -NR<sup>202</sup>-;  
       -S-;  
       -O-;  
       or R<sup>200</sup> represents a bond;

- 10       R<sup>201</sup> represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, methoxymethyl, methoxyethyl,  
methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl,  
propoxypropyl, methoxyphenyl, ethoxyphenyl,  
15       propoxyphenyl, hydroxymethylcarbonyl,  
hydroxyethylcarbonyl, carboxymethylcarbonyl,  
carboxyethylcarbonyl, methoxymethylcarbonyl,  
methoxyethylcarbonyl, ethoxymethylcarbonyl,  
ethoxyethylcarbonyl, methoxyphenylcarbonyl,  
20       ethoxyphenylcarbonyl, amino, aminomethyl, aminoethyl,  
aminopropyl, N-benzylamino, methylaminomethylene,  
aminocarbonyl, methoxycarbonylamino, and  
ethoxycarbonylamino; and

- R<sup>202</sup> is selected from hydrido, methyl phenyl and  
25       benzyl; and

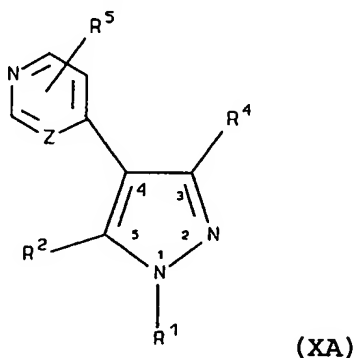
       R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, and methoxy; and

- R<sup>5</sup> is selected from hydrido, methylamino,  
30       dimethylamino, 2-methylbutylamino, ethylamino,  
dimethylaminoethylamino, hydroxypropylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
35       ethyl-2-hydroxy)ethylamino, aminomethyl,  
cyclopropylamino, amino, dimethylaminoethylamino,  
dimethylaminopropylamino, dimethylaminobutylamino,  
dimethylaminopentylamino, diethylaminoethylamino,  
diethylaminopropylamino, diethylaminobutylamino, and

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- 40 diethylaminopentylamino; or  
a pharmaceutically-acceptable salt or tautomer thereof.
104. A compound of Claim 101 wherein:  
R<sup>1</sup> is hydrido; and  
R<sup>2</sup> is R<sup>200</sup>-piperidinyl-R<sup>201</sup> wherein:  
R<sup>200</sup> is selected from:  
5 methylene;  
-NR<sup>202</sup>-;  
-S-;  
-O-;  
or R<sup>200</sup> represents a bond;  
10 R<sup>201</sup> represents one or more radicals selected from  
the group consisting of methoxyethyl, methylcarbonyl,  
hydroxymethylcarbonyl, methoxymethylcarbonyl, and amino;  
and  
R<sup>202</sup> is selected from hydrido and methyl; and  
15 R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, and methoxy; and  
R<sup>5</sup> is selected from hydrido, hydroxypropylamino,  
hydroxycyclohexylamino, diethylaminoethylamino; or  
20 a pharmaceutically-acceptable salt or tautomer thereof.

105. A compound of Claim 94 having the Formula XA:



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wherein:

Z represents a carbon atom or a nitrogen atom; and

5 R<sup>1</sup> is selected from hydrido, methyl, ethyl, hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-piperazinyl-R<sup>201</sup> wherein:

R<sup>200</sup> is selected from:

- (CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

10 -NR<sup>202</sup>-;

-S-;

-O-;

or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from  
15 the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene,  
20 propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,  
25 hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
30 ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl,  
35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene, methylaminoethylene, ethylaminoethylene, aminocarbonyl,

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- 40 methylcarbonylamino, ethylcarbonylamino,  
methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
aminomethylcarbonylamino, carbonylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
45 methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene,  
ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
50 methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
methylsulfonylamino; and  
R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
55 y is 0, 1 or 2; and  
R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and  
60 R<sup>5</sup> is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,  
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,  
methylamino, dimethylamino, 2-methylbutylamino,  
ethylamino, dimethylaminoethylamino, hydroxyethylamino,  
65 hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
hydroxy)ethylamino, piperidinylamino,  
70 pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminoethylamino,

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75 dimethylaminoethylamino, methylaminopropylamino,  
dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,  
dimethylaminopentylamino, ethylaminoethylamino,  
diethylaminoethylamino, ethylaminopropylamino,  
80 diethylaminopropylamino, ethylaminobutylamino,  
diethylaminobutylamino, ethylaminopentylamino,  
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;  
or

a pharmaceutically-acceptable salt or tautomer  
85 thereof.

106. A compound of Claim 105 wherein:

$R^1$  is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

$R^2$  is  $R^{200}$ -piperazinyl- $R^{201}$  wherein:

5  $R^{200}$  is selected from:

$-(CR^{202}R^{203})_y-$ ;

$-NR^{202}-$ ;

$-S-$ ;

$-O-$ ;

10 or  $R^{200}$  represents a bond;

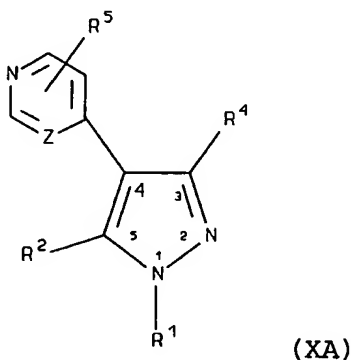
$R^{201}$  represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-  
dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,  
15 cyclohexyl, methoxymethylene, methoxyethylene,  
ethoxyethylene, methoxyphenylene, ethoxyphenylene,  
cyclopropylcarbonyl, cyclobutylcarbonyl,  
cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl,  
chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,  
20 hydroxyethylcarbonyl, hydroxypropylcarbonyl,  
carboxymethylcarbonyl, carboxyethylcarbonyl,  
carboxypropylcarbonyl, methoxymethylcarbonyl,  
methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,

- 25 ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
propoxyphenylcarbonyl, piperidinylmethylcarbonyl,  
piperazinylmethylcarbonyl, morpholinylcarbonyl,  
30 methylsulfonylmethylene, amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,  
methylaminomethylene, ethylaminomethylene,  
methylaminoethylene, ethylaminoethylene, aminocarbonyl,  
methylcarbonylamino, ethylcarbonylamino,  
35 methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
aminomethylcarbonylaminoethylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
40 methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene,  
ethoxycarbonylaminomethylene, and methylsulfonylamino;  
and
- 45  $R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
methyl, ethyl, phenyl and benzyl; and  
y is 0, 1 or 2; and  
 $R^4$  is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
50 selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and  
 $R^5$  is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, cyano, carboxy, methoxy,  
methoxycarbonyl, aminocarbonyl, acetyl, methylamino,  
55 dimethylamino, ethylamino, dimethylaminoethylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
ethyl-2-hydroxy)ethylamino, aminomethyl,  
60 cyclopropylamino, amino, ethoxycarbonylamino,

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methoxyphenylmethylamino, phenylmethylamino,  
 fluorophenylmethylamino, fluorophenylethylamino,  
 methylaminoethylamino, dimethylaminoethylamino,  
 methylaminopropylamino, dimethylaminopropylamino,  
 65 methylaminobutylamino, dimethylaminobutylamino,  
 methylaminopentylamino, dimethylaminopentylamino,  
 ethylaminoethylamino, diethylaminoethylamino,  
 ethylaminopropylamino, diethylaminopropylamino,  
 ethylaminobutylamino, diethylaminobutylamino,  
 70 ethylaminopentylamino, methylaminocarbonyl,  
 methylcarbonyl, and ethylcarbonyl; or  
 a pharmaceutically-acceptable salt or tautomer  
 thereof.

107. A compound of Claim 94 having the Formula XA:



wherein:

Z represents a carbon atom or a nitrogen atom; and

5 R<sup>1</sup> is selected from hydrido, methyl, ethyl,  
 hydroxyethyl and propargyl; and

R<sup>2</sup> is R<sup>200</sup>-cyclohexyl-R<sup>201</sup> wherein:

R<sup>200</sup> is selected from:

-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

10 -NR<sup>202</sup>-;

-S-;



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-O-;

or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from

15 the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethylene, methoxyethylene, methoxypropylene, ethoxyethylene, ethoxypropylene,

20 propoxyethylene, propoxypropylene, methoxyphenylene, ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, benzoyl, chlorobenzoyl, fluorobenzoyl, hydroxymethylcarbonyl,

25 hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxymethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl,

30 ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl,

35 methylsulfonylmethylene, amino, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethylene, ethylaminomethylene, methylaminoethylene, ethylaminoethylene, aminocarbonyl, methylcarbonylamino, ethylcarbonylamino,

40 methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethylene, ethylcarbonylaminomethylene, aminomethylcarbonylaminoethylmethylene, methoxycarbonylamino, ethoxycarbonylamino,

45 methoxymethylcarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethylene,

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ethoxycarbonylaminomethylene, methylimidocarbonyl,  
ethylimidocarbonyl, amidino, methylamidino,  
50 methylamidino, benzylamidino, guanidino,  
guanidinomethylene, guanidinoethylene, and  
methylsulfonylamino; and  
R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido,  
methyl, ethyl, propyl, butyl, phenyl and benzyl; and  
55 y is 0, 1 or 2; and  
R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and  
60 R<sup>5</sup> is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy,  
methoxy, methoxycarbonyl, aminocarbonyl, acetyl,  
methylamino, dimethylamino, 2-methylbutylamino,  
ethylamino, dimethylaminoethylamino, hydroxyethylamino,  
65 hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino,  
imidazolylamino, morpholinylethylamino, (1-ethyl-2-  
hydroxy)ethylamino, piperidinylamino,  
70 pyridinylmethylamino, phenylmethylpiperidinylamino,  
aminomethyl, cyclopropylamino, amino,  
ethoxycarbonylamino, methoxyphenylmethylamino,  
phenylmethylamino, fluorophenylmethylamino,  
fluorophenylethylamino, methylaminoethylamino,  
75 dimethylaminoethylamino, methylaminopropylamino,  
dimethylaminopropylamino, methylaminobutylamino,  
dimethylaminobutylamino, methylaminopentylamino,  
dimethylaminopentylamino, ethylaminoethylamino,  
diethylaminoethylamino, ethylaminopropylamino,  
80 diethylaminopropylamino, ethylaminobutylamino,  
diethylaminobutylamino, ethylaminopentylamino,  
methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl;  
or

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a pharmaceutically-acceptable salt or tautomer  
85 thereof.

108. A compound of Claim 107 wherein:

$R^1$  is selected from hydrido, methyl, ethyl,  
hydroxyethyl and propargyl; and

$R^2$  is  $R^{200}$ -cyclohexyl- $R^{201}$  wherein:

5  $R^{200}$  is selected from:

-  $(CR^{202}R^{203})_y$ -;

- $NR^{202}$ -;

-S-;

-O-;

10 or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from  
the group consisting of hydroxy, hydroxymethyl,  
hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-  
dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl,  
15 cyclohexyl, methoxymethylene, methoxyethylene,  
methoxypropylene, ethoxyethylene, ethoxypropylene,  
propoxyethylene, propoxypropylene, methoxyphenylene,  
ethoxyphenylene, propoxyphenylene, cyclopropylcarbonyl,  
cyclobutylcarbonyl, cyclopentylcarbonyl,  
20 cyclohexylcarbonyl, benzoyl, chlorobenzoyl,  
fluorobenzoyl, hydroxymethylcarbonyl,  
hydroxyethylcarbonyl, hydroxypropylcarbonyl,  
carboxymethylcarbonyl, carboxyethylcarbonyl,  
carboxypropylcarbonyl, methoxymethylcarbonyl,  
25 methoxyethylcarbonyl, methoxypropylcarbonyl,  
ethoxymethylcarbonyl, ethoxyethylcarbonyl,  
ethoxypropylcarbonyl, propoxymethylcarbonyl,  
propoxyethylcarbonyl, propoxypropylcarbonyl,  
methoxyphenylcarbonyl, ethoxyphenylcarbonyl,  
30 propoxyphenylcarbonyl, piperidinylmethylcarbonyl,  
piperazinylmethylcarbonyl, morpholinylcarbonyl,  
methylsulfonylmethylene, amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,

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- methyaminomethylene, ethylaminomethylene,  
35 methylaminoethylene, ethylaminoethylene, aminocarbonyl,  
methylcarbonylamino, ethylcarbonylamino,  
methyaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
40 aminomethylcarbonylaminoethylmethylene,  
methoxycarbonylamino, ethoxycarbonylamino,  
methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene, and  
45 ethoxycarbonylaminomethylene; and  
R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido,  
methyl, ethyl, phenyl and benzyl; and  
y is 0, 1 or 2; and  
R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
50 substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, ethyl, methoxy and  
ethoxy; and  
R<sup>5</sup> is selected from hydrido, fluoro, chloro, bromo,  
hydroxy, methyl, ethyl, cyano, carboxy, methoxy,  
55 methoxycarbonyl, aminocarbonyl, acetyl, methylamino,  
dimethylamino, ethylamino, dimethylaminoethylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
60 ethyl-2-hydroxy)ethylamino, aminomethyl,  
cyclopropylamino, amino, ethoxycarbonylamino,  
methoxyphenylmethylamino, phenylmethylamino,  
fluorophenylmethylamino, fluorophenylethylamino,  
methylaminoethylamino, dimethylaminoethylamino,  
65 methylaminopropylamino, dimethylaminopropylamino,  
methylaminobutylamino, dimethylaminobutylamino,  
methylaminopentylamino, dimethylaminopentylamino,  
ethylaminoethylamino, diethylaminoethylamino,  
ethylaminopropylamino, diethylaminopropylamino,

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70 ethylaminobutylamino, diethylaminobutylamino,  
ethylaminopentylamino, methylaminocarbonyl,  
methylcarbonyl, and ethylcarbonyl; or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

109. A compound of Claim 107 wherein:

R<sup>1</sup> is hydrido; and

R<sup>2</sup> is R<sup>200</sup>-cyclohexyl-R<sup>201</sup> wherein:

R<sup>200</sup> is selected from:

5 methylene;

-NR<sup>202</sup>-;

-S-;

-O-;

or R<sup>200</sup> represents a bond;

10 R<sup>201</sup> represents one or more radicals selected from  
the group consisting of amino, aminomethyl, aminoethyl,  
aminopropyl, phenylamino, benzylamino,  
methylaminomethylene, ethylaminomethylene,  
methylaminoethylene, ethylaminoethylene, aminocarbonyl,  
15 methylcarbonylamino, ethylcarbonylamino,  
methylaminomethylcarbonyl, ethylaminomethylcarbonyl,  
methylcarbonylaminomethylene,  
ethylcarbonylaminomethylene,  
aminomethylcarbonylamino, aminocarbonylmethylene,  
20 methoxycarbonylamino, ethoxycarbonylamino,  
methoxymethylcarbonylamino, methoxyethylcarbonylamino,  
ethoxymethylcarbonylamino, ethoxyethylcarbonylamino,  
methoxycarbonylaminomethylene, and  
ethoxycarbonylaminomethylene; and

25 R<sup>202</sup> is selected from hydrido, methyl, phenyl and  
benzyl; and

R<sup>4</sup> is phenyl, wherein said phenyl is optionally  
substituted with one or more radicals independently  
selected from fluoro, chloro, methyl, and methoxy; and

30 R<sup>5</sup> is selected from hydrido, methylamino,

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dimethylamino, 2-methylbutylamino, ethylamino,  
dimethylaminoethylamino, hydroxypropylamino,  
hydroxyethylamino, hydroxypropylamino, hydroxybutylamino,  
hydroxycyclopropylamino, hydroxycyclobutylamino,  
35 hydroxycyclopentylamino, hydroxycyclohexylamino, (1-  
ethyl-2-hydroxy)ethylamino, aminomethyl,  
cyclopropylamino, amino, dimethylaminoethylamino,  
dimethylaminopropylamino, dimethylaminobutylamino,  
dimethylaminopentylamino, diethylaminoethylamino,  
40 diethylaminopropylamino, diethylaminobutylamino, and  
diethylaminopentylamino; or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

110. A compound of Claim 94 wherein R<sup>2</sup> comprises a  
substituted piperidinyl or piperazinyl moiety with at  
least one substituent attached to the distal nitrogen  
heteroatom or to a carbon ring atom adjacent to the  
5 distal nitrogen heteroatom of the piperidine or  
piperazine ring.

111. A compound Claim 94 wherein R<sup>2</sup> comprises a  
substituted piperidinyl moiety with at least one  
substituent attached to the distal nitrogen heteroatom or  
to a carbon ring atom adjacent to the distal nitrogen  
5 heteroatom of the piperidine ring.

112. A compound of Claim 94 wherein R<sup>2</sup> comprises a  
substituted piperazinyl moiety with at least one  
substituent attached to the distal nitrogen heteroatom or  
to a carbon ring atom adjacent to the distal nitrogen  
5 heteroatom of the piperazine ring.

113. A compound of Claim 94 wherein Z represents a  
carbon atom.

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114. A compound of Claim 94 wherein Z represents a nitrogen atom.

115. A compound of Claim 94 wherein R<sup>1</sup> is hydrido.

116. A compound of Claim 94 wherein R<sup>200</sup> represents a bond.

117. A compound of Claim 94 wherein R<sup>201</sup> represents one or more radicals selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

118. A compound of Claim 94 wherein R<sup>201</sup> represents one or more radicals selected from the group consisting of hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, methylaminomethylene, ethylaminomethylene, methylaminoethylene, and ethylaminoethylene.

119. A compound of Claim 94 wherein R<sup>4</sup> is optionally substituted phenyl.

120. A compound of Claim 94 wherein R<sup>4</sup> is phenyl optionally substituted at a substitutable position with one or more radicals independently selected from chloro, fluoro, bromo and iodo.

121. A compound of Claim 94 wherein R<sup>4</sup> is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

122. A compound of Claim 94 wherein R<sup>5</sup> is hydrido.

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123. A compound of Claim 94 wherein:

R<sup>1</sup> is hydrido;

R<sup>200</sup> represents a bond;

5 R<sup>201</sup> represents one or more radicals selected from  
the group consisting of lower hydroxyalkyl, lower  
hydroxyalkylcarbonyl, and lower alkylaminoalkylene.

R<sup>4</sup> is phenyl optionally substituted at a  
substitutable position with one or more radicals  
independently selected from halo; and

10 R<sup>5</sup> is hydrido.

124. A compound of Claim 94 wherein:

R<sup>1</sup> is hydrido;

R<sup>200</sup> represents a bond;

5 R<sup>201</sup> represents one or more radicals selected from  
the group consisting of hydroxymethyl, hydroxyethyl,  
hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-  
dimethyl)ethyl, hydroxymethylcarbonyl,  
hydroxyethylcarbonyl, hydroxypropylcarbonyl,  
methylaminomethylene, ethylaminomethylene,  
10 methylaminoethylene, and ethylaminoethylene;

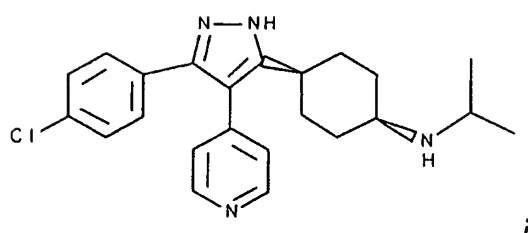
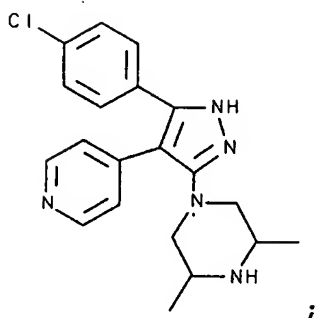
R<sup>4</sup> is phenyl optionally substituted at a  
substitutable position with one or more radicals  
independently selected from chloro, fluoro, bromo and  
iodo; and

15 R<sup>5</sup> is hydrido.

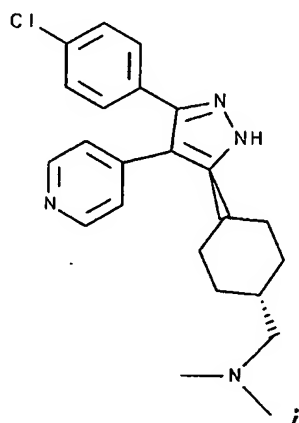
125. A compound selected from compounds, their  
tautomers and their pharmaceutically acceptable salts, of  
the group consisting of:



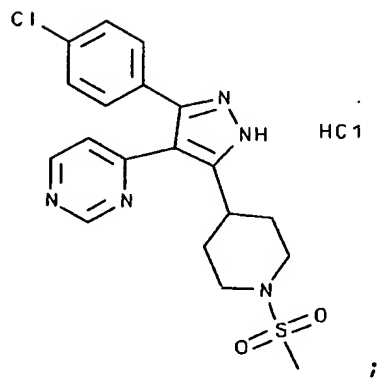
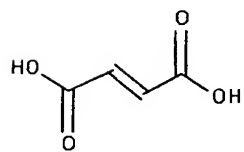
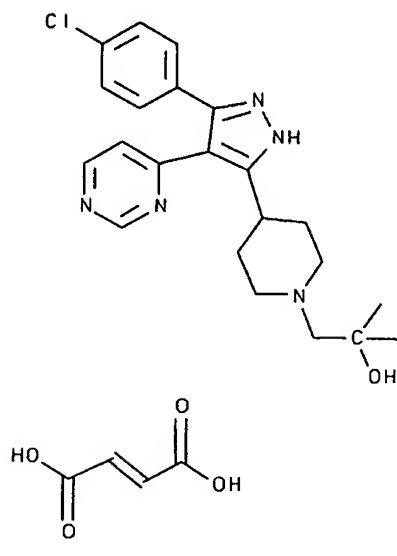
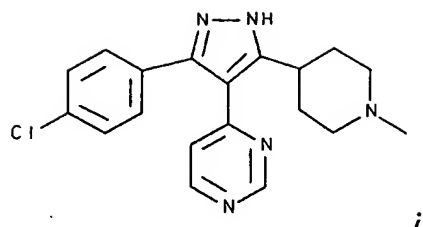
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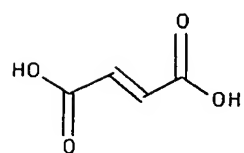
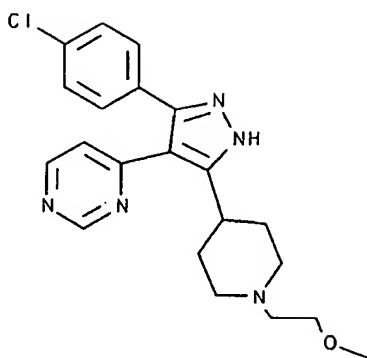
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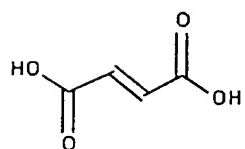
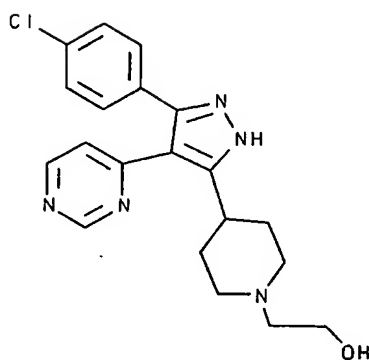


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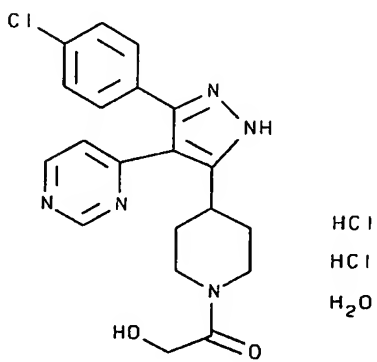
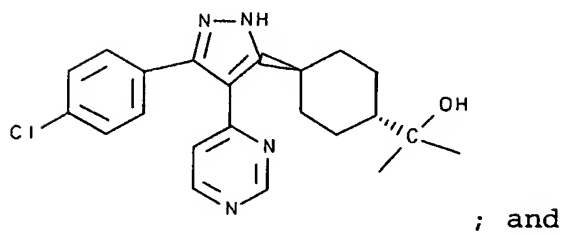
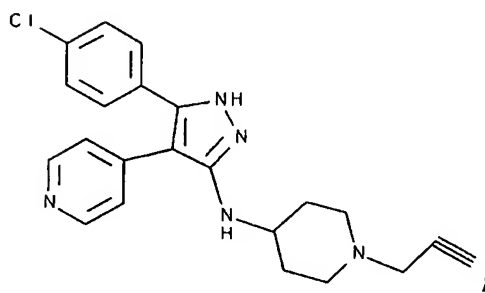
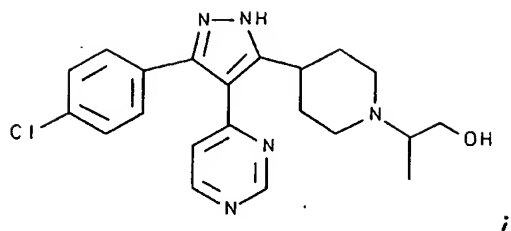
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;



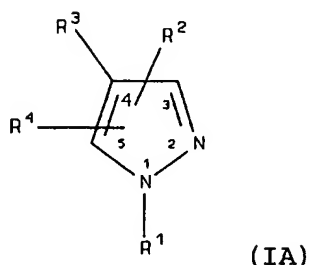
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126. A compound of Formula IA



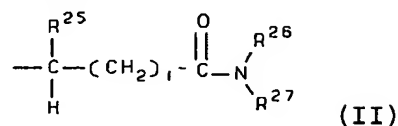
wherein

- 5         $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxyoxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxyoxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, heterocyclylcarbonyloxyarylene,
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- 30 arylcarbonyloxyarylene, and  
heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

- 35 i is an integer from 0 to 9;  
R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
alkylcarbonylalkylene, arylcarbonylalkylene, and  
40 heterocyclylcarbonylaminoalkylene; and  
R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
alkynyl, cycloalkylalkylene, aralkyl,  
alkoxycarbonylalkylene, and alkylaminoalkyl; and  
R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
cycloalkenylalkylene, cycloalkylarylene,  
cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
alkylheterocyclylalkylene, alkylheterocyclylarylene,  
50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
aryloxyarylene, aralkoxyarylene,  
alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,  
55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,  
alkylaminoalkylene, arylaminocarbonylalkylene,  
alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,  
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,  
arylcarbonylalkylene, alkoxycarbonylarylene,  
60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,

alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

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$R^2$  is  $R^{200}$ -cycloalkyl- $R^{201}$  wherein:

100  $R^{200}$  is selected from:

-  $(CR^{202}R^{203})_y-$ ;

-  $C(O)-$ ;

-  $C(O)-(CH_2)_y-$ ;

-  $C(O)-O-(CH_2)_y-$ ;

105 -  $(CH_2)_y-C(O)-$ ;

-  $O-(CH_2)_y-C(O)-$ ;

-  $NR^{202}-$ ;

-  $NR^{202}-(CH_2)_y-$ ;

-  $(CH_2)_y-NR^{202}-$ ;

110 -  $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;

-  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-$ ;

115 -  $(CR^{202}R^{203})_y-S(O)_x-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;

-  $O-(CH_2)_y-$ ;

-  $(CH_2)_y-O-$ ;

120 -  $S-$ ; and

-  $O-$ ;

$R^{201}$  represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,



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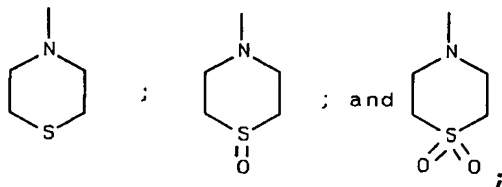
135 alkylaminoalkylcarbonylamino,  
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 140 alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6  
 wherein y + z is less than or equal to 6; and

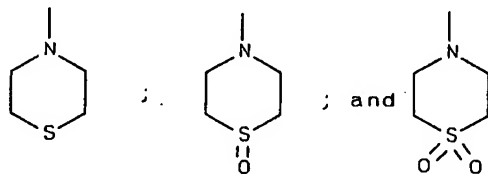
145 x is 0, 1 or 2; and

$R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



150

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



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groups may be optionally substituted with one or more  
 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 160 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 alkenylamino, alkynylamino, cycloalkylamino,  
 cycloalkenylamino, arylamino, haloaryl amino,  
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,

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165 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl,  
alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
170 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
alkylheterocyclylamino, heterocyclylalkylamino,  
alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
heterocyclylheterocyclylalkylamino,  
175 alkoxy carbonylheterocyclylamino, nitro,  
alkylaminocarbonyl, alkylcarbonylamino,  
haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$   
wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or  
180 aralkyl; and

$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,  
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 $R^4$  is optionally substituted with one or more radicals  
independently selected from halo, alkyl, alkenyl,  
185 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
190 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy;

provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl  
195 ring containing a 2-hydroxy substituent and when  $R^1$  is  
hydrido; and

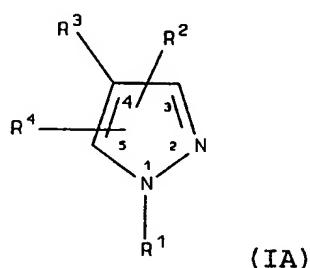
further provided that  $R^4$  is not methylsulfonylphenyl  
or aminosulfonylphenyl; and

further provided that  $R^1$  is not methylsulfonylphenyl;  
200 or

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a pharmaceutically-acceptable salt or tautomer thereof.

127. A compound of Formula IA



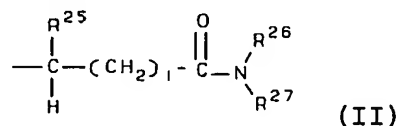
wherein

- 5         $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxy carbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene,
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alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 30 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

35 i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 40 heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxy carbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
 aryloxyarylene, aralkoxyarylene,  
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
 alkoxy carbonylalkylene, alkoxy carbonyl heterocyclyl,  
 55 alkoxy carbonyl heterocyclyl carbonylalkylene, aminoalkyl,  
 alkylaminoalkylene, arylaminocarbonylalkylene,  
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,  
 arylaminocarbonylalkylene, alkylaminocarbonylalkylene,  
 arylcarbonylalkylene, alkoxy carbonylarylene,  
 60 aryloxy carbonylarylene, alkylaryloxy carbonylarylene,

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arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxylarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals

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independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is  $R^{200}$ -aryl- $R^{201}$  wherein:

100  $R^{200}$  is selected from:

-  $(CR^{202}R^{203})_y-$ ;

-C(O)-;

-C(O)-(CH<sub>2</sub>)<sub>y</sub>-;

-C(O)-O-(CH<sub>2</sub>)<sub>y</sub>-;

105 - (CH<sub>2</sub>)<sub>y</sub>-C(O)-;

-O-(CH<sub>2</sub>)<sub>y</sub>-C(O)-;

-NR<sup>202</sup>-;

-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>y</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-NR<sup>300</sup>-;

110 - (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z1</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-C(O)-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-(CH<sub>2</sub>)<sub>z</sub>-;

-(CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-NR<sup>203</sup>-(CH<sub>2</sub>)<sub>z</sub>-;

-S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;

115 - (CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-S(O)<sub>x</sub>-;

-S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-O-;

-S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-C(O)-;

-O-(CH<sub>2</sub>)<sub>y</sub>-;

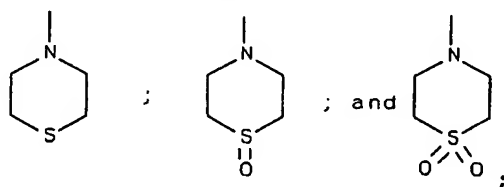
-(CH<sub>2</sub>)<sub>y</sub>-O-; and

120 -O-;

$R^{201}$  represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino,

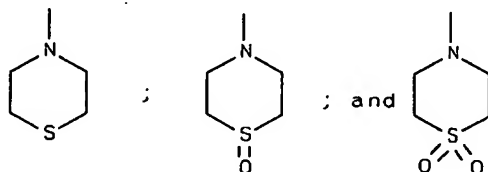
1170

- alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
 alkylaminoalkylcarbonylamino,  
 135 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
 alkoxylalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 alkylsulfonylamino; and  
 140  $R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and  
 $R^{300}$  is selected from alkyl, aryl and aralkyl; and  
 y and z are independently 0, 1, 2, 3, 4, 5 or 6  
 wherein y + z; and y1 is 1, 2, 3, 4, 5 or 6; wherein y +  
 145 z and y1 + z are less than or equal to 6; and  
 x is 0, 1 or 2; and  
 $R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



150

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,



155

- groups may be optionally substituted with one or more  
 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 160 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,

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165 alkenylamino, alkynylamino, cycloalkylamino,  
cycloalkenylamino, arylamino, haloarylamino,  
heterocyclylamino, aminocarbonyl, cyano, hydroxy,  
hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl,  
alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
170 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
alkylheterocyclylamino, heterocyclylalkylamino,  
alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
175 heterocyclylheterocyclylalkylamino,  
alkoxycarbonylheterocyclylamino, nitro,  
alkylaminocarbonyl, alkylcarbonylamino,  
haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$   
180 wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or  
aralkyl; and

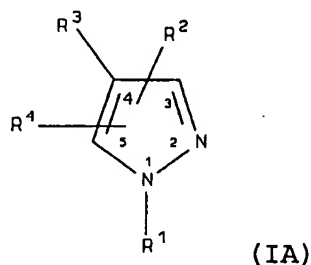
$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,  
cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 $R^4$  is optionally substituted with one or more radicals  
185 independently selected from halo, alkyl, alkenyl,  
alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
190 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy;  
195 provided  $R^3$  is not 2-pyridinyl when  $R^4$  is a phenyl  
ring containing a 2-hydroxy substituent and when  $R^1$  is  
hydrido; and  
further provided that  $R^4$  is not methylsulfonylphenyl



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or aminosulfonylphenyl; and  
 200 further provided that R<sup>1</sup> is not methylsulfonylphenyl;  
 or  
 a pharmaceutically-acceptable salt or tautomer  
 thereof.

128. A compound of Formula IA



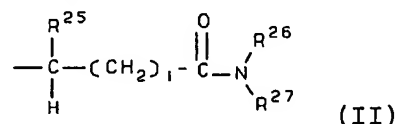
wherein

5 R<sup>1</sup> is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl,  
 10 hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene,  
 15 alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
 20 heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxy carbonylalkylene, aryloxycarbonylalkylene, heterocycliloxy carbonylalkylene, alkoxy carbonylaryl, aryloxycarbonylaryl, heterocycliloxy carbonylaryl,

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- 25 alkylcarbonylalkylene, arylcarbonylalkylene,  
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 30 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

- 35 i is an integer from 0 to 9;  
 R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 40 heterocyclylcarbonylaminoalkylene; and  
 R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxyalkylene, and alkylaminoalkyl; and  
 R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,  
 alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
 aryloxyarylene, aralkoxyarylene,  
 alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
 alkoxyalkoxyalkylene, alkoxyalkoxyheterocyclyl,  
 55 alkoxyalkoxyheterocyclylalkylene, aminoalkyl,  
 alkylaminoalkylene, arylaminocarbonylalkylene,  
 alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene,

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arylaminoacetylalkylene, alkylaminocarbonylalkylene,  
arylcarbonylalkylene, alkoxycarbonylarylene,  
60 aryloxyacetylarylene, alkylaryloxyacetylarylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxyarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxyacetylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and

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alkoxycarbonylamino; wherein said aryl,  
 95 heterocyclylalkylene and aryloxyalkylene radicals may be  
 optionally substituted with one or more radicals  
 independently selected from halogen, alkyl and alkoxy;  
 and

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$  wherein:

100  $R^{200}$  is selected from:

-  $(CR^{301}R^{302})_y-$ ;

-  $C(O)-(CH_2)_{y1}-$ ;

-  $C(O)-O-(CH_2)_y-$ ;

-  $(CH_2)_y-C(O)-$ ;

105 -  $O-(CH_2)_y-C(O)-$ ;

-  $NR^{303}-$ ;

-  $NR^{303}-(CH_2)_y-$ ;

-  $(CH_2)_{y1}-NR^{202}-$ ;

-  $(CH_2)_y-NR^{202}-(CH_2)_{z1}-$ ;

110 -  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;

-  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-$ ;

-  $(CR^{202}R^{203})_y-S(O)_x-$ ;

115 -  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;

-  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;

-  $O-(CH_2)_y-$ ; and

-  $(CH_2)_y-O-$ ;

$R^{201}$  represents one or more radicals selected from  
 120 the group consisting of hydrido, halogen, hydroxy,  
 carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,  
 cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
 aralkyl, heterocyclylalkylene, alkylcarbonyl,  
 hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,  
 125 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,  
 alkoxycarbonyl, carboxyalkylcarbonyl,  
 alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,  
 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,  
 alkylamino, aralkylamino, alkylaminoalkylene,

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- 130 aminocarbonyl, alkylcarbonylamino,  
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
 alkylaminoalkylcarbonylamino,  
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
 alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 135 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and

- 140  $R^{301}$  and  $R^{302}$  are independently selected from aryl and  
 aralkyl; and

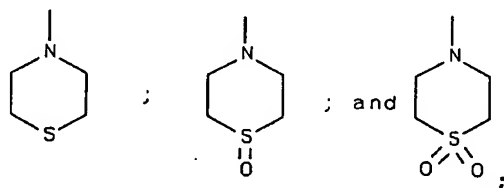
$R^{303}$  is selected from alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6; and  
 y1 is 1, 2, 3, 4, 5 or 6; wherein y + z and y1 + z are

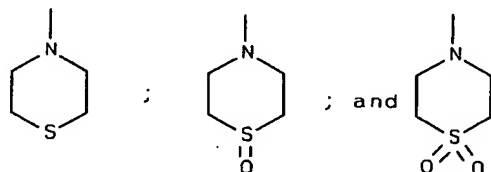
- 145 less than or equal to 6; and

x is 0, 1 or 2; wherein either x or y is other than  
 0 when  $R^{200}$  is  $-S(O)_x-(CR^{202}R^{203})_y-$ ; and

- $R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 150 thiazolylalkyl, thiazolylamino,



- wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl, maleimidyl, pyridonyl, thiazolyl,  
 155 thiazolylalkyl, thiazolylamino,



groups may be optionally substituted with one or more  
 radicals independently selected from halo, keto, alkyl,

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160 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 alkenylamino, alkynylamino, cycloalkylamino,  
 165 cycloalkenylamino, arylamino, haloaryl amino, heterocyclylamino, aminocarbonyl, cyano, hydroxy,  
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
 alkoxycarbonyl, aryloxycarbonyl, heterocyclylalkoxycarbonyl,  
 170 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
 alkylheterocyclylamino, heterocyclylalkylamino,  
 175 alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
 heterocyclylheterocyclylalkylamino,  
 alkoxycarbonylheterocyclylamino, nitro,  
 alkylaminocarbonyl, alkylcarbonylamino,  
 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
 180 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR<sup>44</sup>R<sup>45</sup>  
 wherein R<sup>44</sup> is alkylcarbonyl or amino, and R<sup>45</sup> is alkyl or  
 aralkyl; and

R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl,  
 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 185 R<sup>4</sup> is optionally substituted with one or more radicals  
 independently selected from halo, alkyl, alkenyl,  
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
 alkylsulfinylalkylene, arylsulfinylalkylene,  
 190 alkylsulfonyl, alkylsulfonylalkylene,  
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
 nitro, alkylamino, arylamino, alkylaminoalkylene,  
 195 arylaminoalkylene, aminoalkylamino, and hydroxy;

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provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl ring containing a 2-hydroxy substituent and when R<sup>1</sup> is hydrido; and

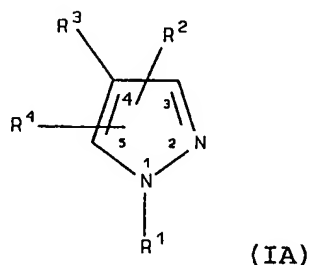
200 further provided R<sup>2</sup> is selected from aryl, heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl when R<sup>4</sup> is hydrido; and

further provided that R<sup>4</sup> is not methylsulfonylphenyl or aminosulfonylphenyl; and

205 or further provided that R<sup>1</sup> is not methylsulfonylphenyl;

a pharmaceutically-acceptable salt or tautomer thereof.

129. A compound of Formula IA



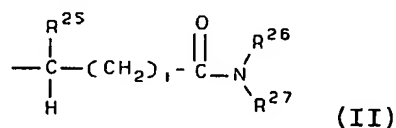
wherein

5 R<sup>1</sup> is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, 10 alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl,

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arylsulfinyl, heterocyclisulfinyl, alkylsulfonyl,  
 alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl,  
 20 heterocyclisulfonyl, alkylaminoalkylene,  
 alkylsulfonylalkylene, acyl, acyloxycarbonyl,  
 alkoxycarbonylalkylene, aryloxycarbonylalkylene,  
 heterocyclioxycarbonylalkylene, alkoxycarbonylarylene,  
 aryloxycarbonylarylene, heterocyclioxycarbonylarylene,  
 25 alkylcarbonylalkylene, arylcarbonylalkylene,  
 heterocyclylcarbonylalkylene, alkylcarbonylarylene,  
 arylcarbonylarylene, heterocyclylcarbonylarylene,  
 alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene,  
 heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene,  
 30 arylcarbonyloxyarylene, and  
 heterocyclylcarbonyloxyarylene; or

R<sup>1</sup> has the formula



wherein:

35 i is an integer from 0 to 9;

R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 alkylcarbonylalkylene, arylcarbonylalkylene, and  
 40 heterocyclylcarbonylaminoalkylene; and

R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl,  
 alkynyl, cycloalkylalkylene, aralkyl,  
 alkoxycarbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
 45 aryl, heterocyclyl, aralkyl, cycloalkylalkylene,  
 cycloalkenylalkylene, cycloalkylarylene,  
 cycloalkylcycloalkyl, heterocyclylalkylene, alkylarylene,  
 alkylaralkyl, aralkylarylene, alkylheterocyclyl,  
 alkylheterocyclylalkylene, alkylheterocyclylarylene,  
 50 aralkylheterocyclyl, alkoxyalkylene, alkoxyarylene,



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alkoxyaralkyl, alkoxyheterocyclyl, alkoxyalkoxyarylene,  
aryloxyarylene, aralkoxyarylene,  
alkoxyheterocyclylalkylene, aryloxyalkoxyarylene,  
alkoxycarbonylalkylene, alkoxycarbonylheterocyclyl,  
55 alkoxycarbonylheterocyclylcarbonylalkylene, aminoalkyl,  
alkylaminoalkylene, arylaminocarbonylalkylene,  
alkoxyarylaminoalkylene, aminocarbonylalkylene,  
arylaminocarbonylalkylene, alkylaminocarbonylalkylene,  
arylcarbonylalkylene, alkoxycarbonylarylene,  
60 aryloxycarbonylarylene, alkylaryloxycarbonylarylene,  
arylcarbonylarylene, alkylarylcarbonylarylene,  
alkoxycarbonylheterocyclylarylene,  
alkoxycarbonylalkoxyarylene,  
heterocyclylcarbonylalkylarylene, alkylthioalkylene,  
65 cycloalkylthioalkylene, alkylthioarylene,  
aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which

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they are attached form a heterocycle, wherein said heterocycle is optionally substituted with one or more radicals independently selected from alkyl, aryl, heterocyclyl, heterocyclylalkylene, alkylheterocyclylalkylene, aryloxyalkylene, alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl, alkoxycarbonyl, aralkoxycarbonyl, alkylamino and alkoxycarbonylamino; wherein said aryl, heterocyclylalkylene and aryloxyalkylene radicals may be optionally substituted with one or more radicals independently selected from halogen, alkyl and alkoxy; and

$R^2$  is selected from hydrido, halogen, mercapto, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, aralkyl, alkylheterocyclyl, heterocyclylalkyl, heterocyclylheterocyclyl, heterocyclylalkylheterocyclyl, alkylamino, alkenylamino, alkynylamino, arylamino, aryl(hydroxyalkyl)amino, heterocyclylamino, heterocyclylalkylamino, aralkylamino, N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl, aminoalkylamino, aminocarbonylalkylene, arylaminoalkylene, alkylaminoalkylene, arylaminoarylene, alkylaminoarylene, alkylaminoalkylamino, alkylcarbonylaminoalkylene, aminoalkylcarbonylaminoalkylene, alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl, aminoalkylthio, alkylaminocarbonylalkylthio, alkylaminoalkylaminocarbonylalkylthio, alkoxy, heterocyclylthio, alkylthio, cyanoalkylthio, alkenylthio, alkynylthio, carboxyalkylthio, arylthio, heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl, alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylalkylamino, alkoxycarbonylheterocyclyl,

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alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
 125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,  
 aralkythio, heterocyclylalkylthio, aminoalkoxy,  
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein  
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and  
 130 cycloalkenyl groups may be optionally substituted with  
 one or more radicals independently selected from halo,  
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
 aralkyl, heterocyclylalkyl, epoxyalkyl,  
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,  
 135 haloalkyl, alkylamino, alkynylamino,  
 alkylaminoalkylamino, heterocyclylalkylamino,  
 alkylcarbonyl, alkoxy carbonyl, alkylsulfonyl,  
 arylsulfonyl, and aralkylsulfonyl; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 140 cycloalkyl- $R^{201}$  wherein:

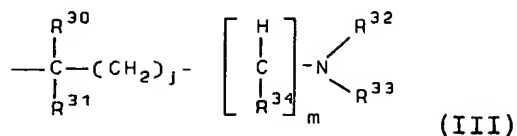
$R^{200}$  is selected from:

- $(CR^{202}R^{203})_y-$ ;
- $C(O)-$ ;
- $C(O)-(CH_2)_y-$ ;
- 145 -  $C(O)-O-(CH_2)_y-$ ;
- $(CH_2)_y-C(O)-$ ;
- $O-(CH_2)_y-C(O)-$ ;
- $NR^{202}-$ ;
- $NR^{202}-(CH_2)_y-$ ;
- 150 -  $(CH_2)_y-NR^{202}-$ ;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;
- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;
- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;
- 155 -  $S(O)_x-(CR^{202}R^{203})_y-$ ;
- $(CR^{202}R^{203})_y-S(O)_x-$ ;
- $S(O)_x-(CR^{202}R^{203})_y-O-$ ;
- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;

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- O-(CH<sub>2</sub>)<sub>y</sub>-;  
 160 - (CH<sub>2</sub>)<sub>y</sub>-O-;  
 -S-;  
 -O-;  
 or R<sup>200</sup> represents a bond;  
 R<sup>201</sup> represents one or more radicals selected from  
 165 the group consisting of hydrido, halogen, hydroxy,  
 carboxy, keto, alkyl, hydroxyalkyl, haloalkyl,  
 cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
 aralkyl, heterocyclylalkylene, alkylcarbonyl,  
 hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,  
 170 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene,  
 alkoxy carbonyl, carboxyalkylcarbonyl,  
 alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl,  
 alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,  
 alkylamino, aralkylamino, alkylaminoalkylene,  
 175 aminocarbonyl, alkylcarbonylamino,  
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
 alkylaminoalkylcarbonylamino,  
 aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino,  
 alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene,  
 180 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 alkylsulfonylamino; and  
 R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and  
 185 y and z are independently 0, 1, 2, 3, 4, 5 or 6  
 wherein y + z is less than or equal to 6; and  
 x is 0, 1 or 2; or  
 R<sup>2</sup> is -NHCR<sup>204</sup>R<sup>205</sup> wherein R<sup>204</sup> is alkylaminoalkylene,  
 and R<sup>205</sup> is aryl; or  
 190 R<sup>2</sup> is -C(NR<sup>206</sup>)R<sup>207</sup> wherein R<sup>206</sup> is selected from  
 hydrogen and hydroxy, and R<sup>207</sup> is selected from alkyl,  
 aryl and aralkyl; or  
 R<sup>2</sup> has the formula:

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195 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

200 R<sup>30</sup> and R<sup>31</sup> are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

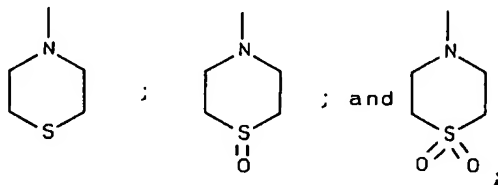
205 R<sup>32</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclylcarbonylaminoalkylene;

210 R<sup>33</sup> is selected from hydrogen, alkyl, -C(O)R<sup>35</sup>, -C(O)OR<sup>35</sup>, -SO<sub>2</sub>R<sup>36</sup>, -C(O)NR<sup>37</sup>R<sup>38</sup>, and -SO<sub>2</sub>NR<sup>39</sup>R<sup>40</sup>, wherein R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup>, R<sup>38</sup>, R<sup>39</sup> and R<sup>40</sup> are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

R<sup>34</sup> is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

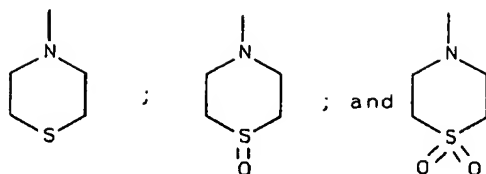
215 R<sup>2</sup> is -CR<sup>41</sup>R<sup>42</sup> wherein R<sup>41</sup> is aryl, and R<sup>42</sup> is hydroxy; and

R<sup>3</sup> is selected from maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



220 wherein the R<sup>3</sup> maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

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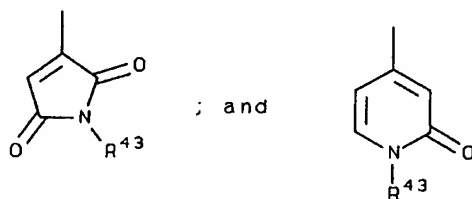


groups may be optionally substituted with one or more  
 225 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 230 alkenylamino, alkynylamino, cycloalkylamino,  
 cycloalkenylamino, arylamino, haloarylamino,  
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,  
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
 235 alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl,  
 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
 240 alkylheterocyclylamino, heterocyclylalkylamino,  
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
 heterocyclylheterocyclylalkylamino,  
 alkoxycarbonylheterocyclylamino, nitro,  
 alkylaminocarbonyl, alkylcarbonylamino,  
 245 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$   
 wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or  
 aralkyl; and

$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl,  
 250 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 $R^4$  is optionally substituted with one or more radicals  
 independently selected from halo, alkyl, alkenyl,  
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

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- 255 alkylsulfinylalkylene, arylsulfinylalkylene,  
 alkylsulfonyl, alkylsulfonylalkylene,  
 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
 aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
 alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
 260 nitro, alkylamino, arylamino, alkylaminoalkylene,  
 arylaminoalkylene, aminoalkylamino, and hydroxy;  
 provided  $R^3$  is not



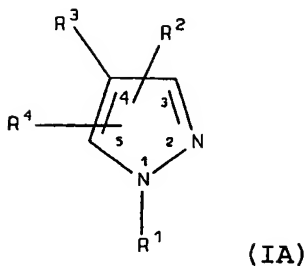
(IV)

(V)

- 265 wherein  $R^{43}$  is selected from hydrogen, alkyl,  
 aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;  
 and  
 further provided  $R^2$  is selected from aryl,  
 heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl  
 270 when  $R^4$  is hydrido; and  
 further provided that  $R^4$  is not methylsulfonylphenyl  
 or aminosulfonylphenyl; and  
 further provided that  $R^1$  is not methylsulfonylphenyl;  
 or  
 275 a pharmaceutically-acceptable salt or tautomer  
 thereof.

130. A compound of Formula IA

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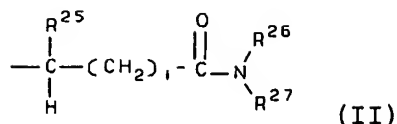
wherein

- 5         $R^1$  is selected from hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocycliloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxycarbonyl, alkoxycarbonylalkylene, aryloxycarbonylalkylene, heterocycliloxycarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, heterocycliloxycarbonylarylene, alkylcarbonylalkylene, arylcarbonylalkylene, heterocyclylcarbonylalkylene, alkylcarbonylarylene, arylcarbonylarylene, heterocyclylcarbonylarylene, alkylcarbonyloxyalkylene, arylcarbonyloxyalkylene, heterocyclylcarbonyloxyalkylene, alkylcarbonyloxyarylene, arylcarbonyloxyarylene, and heterocyclylcarbonyloxyarylene; or

$R^1$  has the formula



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wherein:

35           i is an integer from 0 to 9;

          R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and  
40 heterocyclcarbonylaminoalkylene; and

          R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxyalkylene, and alkylaminoalkyl; and

          R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl,  
45 aryl, heterocycl, aralkyl, cycloalkylalkylene, cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene, aralkylheterocycl,  
50 alkoxyalkylene, alkoxyarylene, alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxyalkylene, alkoxyalkylheterocycl, alkoxyalkylheterocyclcarbonylalkylene, aminoalkyl, alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxyalkylarylene,  
55 aryloxyalkylarylene, alkylaryloxyalkylarylene, arylcarbonylarylene, alkylarylcarbonylarylene, alkoxyalkylheterocyclarylene, alkoxyalkylalkoxyalkylarylene, heterocyclcarbonylalkylarylene, alkylthioalkylene,  
60 cycloalkylthioalkylene, alkylthioarylene,

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aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, alkylaminosulfonylarylene; wherein  
said alkyl, cycloalkyl, aryl, heterocyclyl, aralkyl,  
70 heterocyclylalkylene, alkylheterocyclylarylene,  
alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
75 may be optionally substituted with one or more radicals  
independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-CHR^{28}R^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
80 heterocyclylalkylene, alkylheterocyclylalkylene,  
alkoxycarbonylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
85 and nitro; or

$R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
90 heterocyclyl, heterocyclylalkylene,  
alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
95 heterocyclylalkylene and aryloxyalkylene radicals may be  
optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is selected from hydrido, halogen, mercapto,  
100 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,  
hydroxyalkyl, aralkyl, alkylheterocyclyl,

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heterocyclylalkyl, heterocyclylheterocyclyl,  
heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,  
alkynylamino, arylamino, aryl(hydroxyalkyl)amino,  
105 heterocyclylamino, heterocyclylalkylamino, aralkylamino,  
N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,  
aminoalkylamino, aminocarbonylalkylene,  
arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,  
alkylaminoarylene, alkylaminoalkylamino,  
110 alkylcarbonylaminoalkylene,  
aminoalkylcarbonylaminoalkylene,  
alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,  
aminoalkylthio, alkylaminocarbonylalkylthio,  
alkylaminoalkylaminocarbonylalkylthio, alkoxy,  
115 heterocycliloxy, alkylthio, cyanoalkylthio, alkenylthio,  
alkynylthio, carboxyalkylthio, arylthio,  
heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,  
alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,  
alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,  
120 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,  
alkoxycarbonylalkyl, alkoxycarbonylalkylamino,  
alkoxycarbonylheterocyclyl,  
alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
125 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,  
aralkylthio, heterocyclylalkylthio, aminoalkoxy,  
cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein  
the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and  
130 cycloalkenyl groups may be optionally substituted with  
one or more radicals independently selected from halo,  
keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
aralkyl, heterocyclylalkyl, epoxyalkyl,  
amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,  
135 haloalkyl, alkylamino, alkynylamino,  
alkylaminoalkylamino, heterocyclylalkylamino,  
alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,

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arylsulfonyl, and aralkylsulfonyl; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -cycloalkyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

- $(CR^{202}R^{203})_y-$ ;
- $C(O)-$ ;
- $C(O)-(CH_2)_y-$ ;
- 145 -  $C(O)-O-(CH_2)_y-$ ;
- $(CH_2)_y-C(O)-$ ;
- $O-(CH_2)_y-C(O)-$ ;
- $NR^{202}-$ ;
- $NR^{202}-(CH_2)_y-$ ;
- 150 -  $(CH_2)_y-NR^{202}-$ ;
- $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;
- $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;
- $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;
- $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;
- 155 -  $S(O)_x-(CR^{202}R^{203})_y-$ ;
- $(CR^{202}R^{203})_y-S(O)_x-$ ;
- $S(O)_x-(CR^{202}R^{203})_y-O-$ ;
- $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;
- $O-(CH_2)_y-$ ;
- 160 -  $(CH_2)_y-O-$ ;
- $S-$ ; and
- $O-$ ;

or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from

165 the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl,

170 haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl,

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alkylamino, aralkylamino, alkylaminoalkylene,  
 175 aminocarbonyl, alkylcarbonylamino,  
 alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl,  
 alkylaminoalkylcarbonylamino,  
 aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino,  
 alkoxylalkylcarbonylamino, alkoxycarbonylaminoalkylene,  
 180 alkylimidocarbonyl, amidino, alkylamidino,  
 aralkylamidino, guanidino, guanidinoalkylene, and  
 alkylsulfonylamino; and

$R^{202}$  and  $R^{203}$  are independently selected from hydrido,  
 alkyl, aryl and aralkyl; and

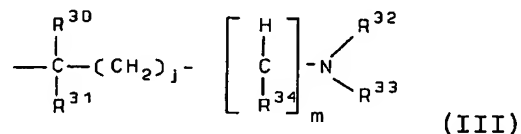
185 y and z are independently 0, 1, 2, 3, 4, 5 or 6  
 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

$R^2$  is  $-NHCR^{204}R^{205}$  wherein  $R^{204}$  is alkylaminoalkylene,  
 and  $R^{205}$  is aryl; or

190  $R^2$  is  $-C(NR^{206})R^{207}$  wherein  $R^{206}$  is selected from  
 hydrogen and hydroxy, and  $R^{207}$  is selected from alkyl,  
 aryl and aralkyl; or

$R^2$  has the formula:



195 wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

$R^{30}$  and  $R^{31}$  are independently selected from hydrogen,  
 alkyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene,  
 200 aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,  
 alkoxyalkyl, and alkylcarbonyloxyalkyl; and

$R^{32}$  is selected from hydrogen, alkyl, aralkyl,  
 heterocyclylalkyl, alkoxyalkylene, aryloxyalkylene,  
 aminoalkyl, alkylaminoalkyl, arylaminoalkyl,  
 205 alkylcarbonylalkylene, arylcarbonylalkylene, and

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heterocyclylcarbonylaminoalkylene;

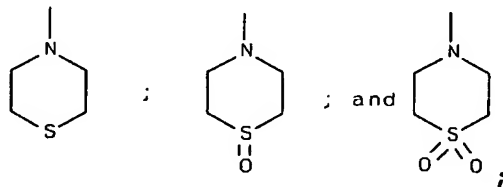
$R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  
 $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ ,  
 wherein

210  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently  
 selected from hydrocarbon, heterosubstituted hydrocarbon  
 and heterocyclyl; and

$R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl,  
 alkylaminocarbonyl, and arylaminocarbonyl; or

215  $R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy;  
 and

$R^3$  is selected from pyridinyl, pyrimidinyl,  
 quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,

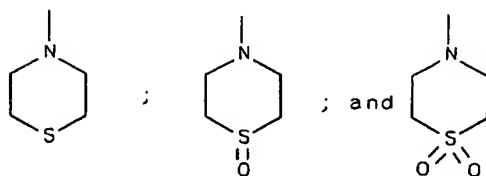


220

wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl,  
 purinyl groups are substituted with one or more radicals  
 independently selected from keto, haloarylamino,  
 225 alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl,  
 alkoxyalkylamino, alkylaminoalkoxy, alkoxyarylamino,  
 alkylsulfonylamino, aryl(hydroxyalkyl)amino,  
 alkylaminoalkylaminoalkylamino, alkylheterocyclylamino,  
 alkylheterocyclylalkylamino,  
 230 heterocyclylheterocyclylalkylamino,  
 alkoxyacylheterocyclylamino and haloalkylsulfonyl;  
 and

wherein the  $R^3$  maleimidyl, pyridonyl, thiazolyl,  
 thiazolylalkyl, thiazolylamino,

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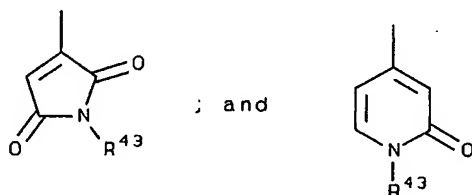
groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR<sup>44</sup>R<sup>45</sup> wherein R<sup>44</sup> is alkylcarbonyl or amino, and R<sup>45</sup> is alkyl or aralkyl; and

R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein R<sup>4</sup> is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

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- alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
270 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy;  
275 provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl  
ring containing a 2-hydroxy substituent and when R<sup>1</sup> is  
hydrido; and  
provided R<sup>3</sup> is not

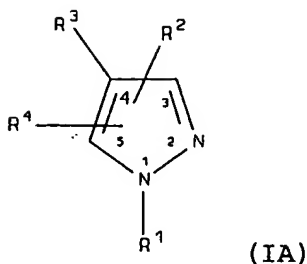


- 280 (IV) (V)  
wherein R<sup>43</sup> is selected from hydrogen, alkyl,  
aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl;  
and  
further provided R<sup>2</sup> is selected from aryl,  
285 heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl  
when R<sup>4</sup> is hydrido; and  
further provided that R<sup>4</sup> is not methylsulfonylphenyl  
or aminosulfonylphenyl; and  
further provided that R<sup>1</sup> is not methylsulfonylphenyl;  
290 or  
a pharmaceutically-acceptable salt or tautomer  
thereof.

131. A compound of Formula IA



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wherein

- 5         $R^1$  is selected from hydroxy and alkoxyaryl; and  
        $R^2$  is selected from hydrido, halogen, mercapto,  
 alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl,  
 hydroxyalkyl, aralkyl, alkylheterocyclyl,  
 heterocyclylalkyl, heterocyclylheterocyclyl,  
 10 heterocyclylalkylheterocyclyl, alkylamino, alkenylamino,  
 alkynylamino, arylamino, aryl(hydroxyalkyl)amino,  
 heterocyclylamino, heterocyclylalkylamino, aralkylamino,  
 N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl,  
 aminoalkylamino, aminocarbonylalkylene,  
 15 arylaminoalkylene, alkylaminoalkylene, arylaminoarylene,  
 alkylaminoarylene, alkylaminoalkylamino,  
 alkylcarbonylaminoalkylene,  
 aminoalkylcarbonylaminoalkylene,  
 alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl,  
 20 aminoalkylthio, alkylaminocarbonylalkylthio,  
 alkylaminoalkylaminocarbonylalkylthio, alkoxy,  
 heterocycloxy, alkylthio, cyanoalkylthio, alkenylthio,  
 alkynylthio, carboxyalkylthio, arylthio,  
 heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl,  
 25 alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl,  
 alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl,  
 carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl,  
 alkoxycarbonylalkyl, alkoxycarbonylalkylamino,  
 alkoxycarbonylheterocyclyl,  
 30 alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino,  
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
 alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl,

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aralkythio, heterocyclylalkylthio, aminoalkoxy,  
 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 35 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; wherein  
 the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl and  
 cycloalkenyl groups may be optionally substituted with  
 one or more radicals independently selected from halo,  
 keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl,  
 40 aralkyl, heterocyclylalkyl, epoxyalkyl,  
 amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, aralkoxy,  
 haloalkyl, alkylamino, alkynylamino,  
 alkylaminoalkylamino, heterocyclylalkylamino,  
 alkylcarbonyl, alkoxycarbonyl, alkylsulfonyl,  
 45 arylsulfonyl, and aralkylsulfonyl; or

$R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 cycloalkyl- $R^{201}$  wherein:

$R^{200}$  is selected from:

- $(CR^{202}R^{203})_y-$ ;
- 50 -C(O)-;
- C(O)-(CH<sub>2</sub>)<sub>y</sub>-;
- C(O)-O-(CH<sub>2</sub>)<sub>y</sub>-;
- 55 - (CH<sub>2</sub>)<sub>y</sub>-C(O)-;
- O-(CH<sub>2</sub>)<sub>y</sub>-C(O)-;
- NR<sup>202</sup>-;
- NR<sup>202</sup>-(CH<sub>2</sub>)<sub>y</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-;
- (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-C(O)-NR<sup>202</sup>-(CH<sub>2</sub>)<sub>z</sub>-;
- 60 - (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-(CH<sub>2</sub>)<sub>z</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-NR<sup>202</sup>-C(O)-NR<sup>203</sup>-(CH<sub>2</sub>)<sub>z</sub>-;
- S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-;
- (CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-S(O)<sub>x</sub>-;
- S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-O-;
- 65 -S(O)<sub>x</sub>-(CR<sup>202</sup>R<sup>203</sup>)<sub>y</sub>-C(O)-;
- O-(CH<sub>2</sub>)<sub>y</sub>-;
- (CH<sub>2</sub>)<sub>y</sub>-O-;
- S-; and

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-O-;

70 or R<sup>200</sup> represents a bond;

R<sup>201</sup> represents one or more radicals selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, aralkyl, heterocyclylalkylene, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkylene, alkoxyarylene, alkoxy carbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonyl, alkylsulfonylalkylene, amino, aminoalkyl, alkylamino, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino, alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

90 R<sup>202</sup> and R<sup>203</sup> are independently selected from hydrido, alkyl, aryl and aralkyl; and

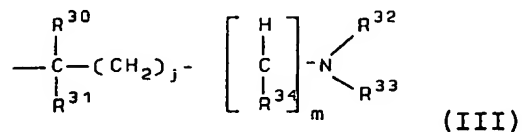
y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and

x is 0, 1 or 2; or

95 R<sup>2</sup> is -NHCR<sup>204</sup>R<sup>205</sup> wherein R<sup>204</sup> is alkylaminoalkylene, and R<sup>205</sup> is aryl; or

R<sup>2</sup> is -C(NR<sup>206</sup>)R<sup>207</sup> wherein R<sup>206</sup> is selected from hydrogen and hydroxy, and R<sup>207</sup> is selected from alkyl, aryl and aralkyl; or

100 R<sup>2</sup> has the formula:



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wherein:

j is an integer from 0 to 8; and

m is 0 or 1; and

105  $R^{30}$  and  $R^{31}$  are independently selected from hydrogen, alkyl, aryl, heterocyclyl, aralkyl, heterocyclalkylene, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

110  $R^{32}$  is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclalkylcarbonylaminoalkylene;

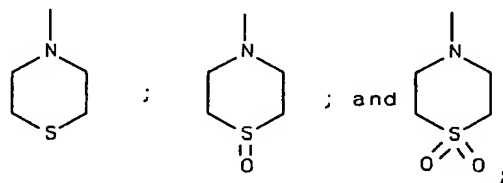
115  $R^{33}$  is selected from hydrogen, alkyl,  $-C(O)R^{35}$ ,  $-C(O)OR^{35}$ ,  $-SO_2R^{36}$ ,  $-C(O)NR^{37}R^{38}$ , and  $-SO_2NR^{39}R^{40}$ , wherein

$R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$  and  $R^{40}$  are independently selected from hydrocarbon, heterosubstituted hydrocarbon and heterocyclyl; and

120  $R^{34}$  is selected from hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; or

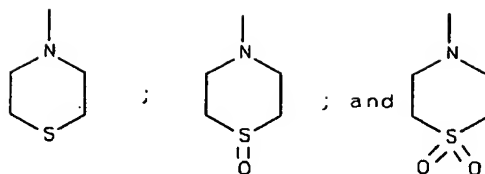
$R^2$  is  $-CR^{41}R^{42}$  wherein  $R^{41}$  is aryl, and  $R^{42}$  is hydroxy; and

125  $R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



130 wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

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groups may be optionally substituted with one or more  
 135 radicals independently selected from halo, keto, alkyl,  
 aralkyl, aralkenyl, arylheterocyclyl, carboxy,  
 carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio,  
 alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl,  
 aralkoxy, heterocyclylalkoxy, amino, alkylamino,  
 140 alkenylamino, alkynylamino, cycloalkylamino,  
 cycloalkenylamino, arylamino, haloarylamino,  
 heterocyclylamino, aminocarbonyl, cyano, hydroxy,  
 hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene,  
 aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy,  
 145 alkoxycarbonyl, aryloxcarbonyl, heterocyclylloxycarbonyl,  
 alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino,  
 aminosulfinyl, aminosulfonyl, alkylsulfonylamino,  
 alkylaminoalkylamino, hydroxyalkylamino, aralkylamino,  
 aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino,  
 150 alkylheterocyclylamino, heterocyclylalkylamino,  
 alkylheterocyclylalkylamino, aralkylheterocyclylamino,  
 heterocyclylheterocyclylalkylamino,  
 alkoxycarbonylheterocyclylamino, nitro,  
 alkylaminocarbonyl, alkylcarbonylamino,  
 155 haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl,  
 hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -NR<sup>44</sup>R<sup>45</sup>  
 wherein R<sup>44</sup> is alkylcarbonyl or amino, and R<sup>45</sup> is alkyl or  
 aralkyl; and

R<sup>4</sup> is selected from hydrido, alkyl, alkenyl, alkynyl,  
 160 cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  
 R<sup>4</sup> is optionally substituted with one or more radicals  
 independently selected from halo, alkyl, alkenyl,  
 alkynyl, aryl, heterocyclyl, alkylthio, arylthio,  
 alkylthioalkylene, arylthioalkylene, alkylsulfinyl,

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- 165 alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
170 nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy;  
provided R<sup>3</sup> is not 2-pyridinyl when R<sup>4</sup> is a phenyl  
ring containing a 2-hydroxy substituent and when R<sup>1</sup> is  
hydrido; and  
175 further provided R<sup>2</sup> is selected from aryl,  
heterocyclyl, unsubstituted cycloalkyl and cycloalkenyl  
when R<sup>4</sup> is hydrido; and  
further provided that R<sup>4</sup> is not methylsulfonylphenyl  
or aminosulfonylphenyl; or  
180 a pharmaceutically-acceptable salt or tautomer  
thereof.

132. A pharmaceutical composition comprising a  
therapeutically-effective amount of a compound, said  
compound selected from the compounds of any one of Claims  
1, 39, 71, 82 and 94, or a pharmaceutically acceptable  
5 salt thereof.

133. A method of treating a TNF mediated disorder,  
said method comprising treating the subject having or  
susceptible to such disorder with a therapeutically-  
effective amount of a compound, said compound selected  
from the compounds of any one of Claims 1, 39, 71, 82 and  
5 94, or a pharmaceutically acceptable salt thereof.

134. A method of treating a p38 kinase mediated  
disorder, said method comprising treating the subject  
having or susceptible to such disorder with a  
therapeutically-effective amount of a compound, said  
compound selected from the compounds of any one of Claims

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5 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

135. The method of Claim 134 wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid  
5 arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis,  
10 inflammatory bowel disease and cachexia.

136. The method of Claim 134 wherein the p38 kinase mediated disorder is inflammation.

137. The method of Claim 134 wherein the p38 kinase mediated disorder is arthritis.

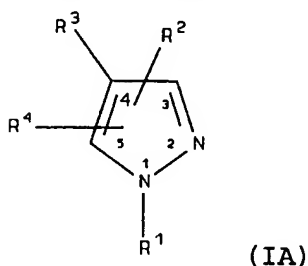
138. The method of Claim 134 wherein the p38 kinase mediated disorder is asthma.

139. A method of treating inflammation, said method comprising treating the subject having or susceptible to inflammation with a therapeutically-effective amount of a compound, said compound selected from the compounds of  
5 any one of Claims 1, 39, 71, 82 and 94, or a pharmaceutically acceptable salt thereof.

140. A method of treating arthritis, said method comprising treating the subject having or susceptible to arthritis with a therapeutically-effective amount of a compound, said compound selected from the compounds of any one of Claims 1, 39, 71, 82 and 94, or a  
5 pharmaceutically acceptable salt thereof.

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141. A method of preparing pyrazoles of Formula IA



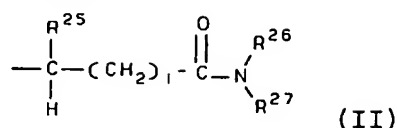
wherein

- $R^1$  is selected from hydrido, hydroxy, alkyl,
- 5 cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkylene, cycloalkenylalkylene, heterocyclylalkylene, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, aralkyl, aralkenyl, aralkynyl,
- 10 arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkylene, alkenylthioalkylene, alkylthioalkenylene, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino,
- 15 alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkylene, alkylsulfonylalkylene, acyl, acyloxy carbonyl, alkoxy carbonylalkylene, aryloxy carbonylalkylene, heterocyclyloxy carbonylalkylene, alkoxy carbonylarylene, aryloxy carbonylarylene, heterocyclyloxy carbonylarylene, alkyl carbonylalkylene, aryl carbonylalkylene,
- 20 heterocyclyl carbonylalkylene, alkyl carbonylarylene, aryl carbonylarylene, heterocyclyl carbonylarylene, alkyl carbonyloxyalkylene, aryl carbonyloxyalkylene, heterocyclyl carbonyloxyalkylene, alkyl carbonyloxyarylene, aryl carbonyloxyarylene, and
- 25 heterocyclyl carbonyloxyarylene; or
- 30



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R<sup>1</sup> has the formula



wherein:

i is an integer from 0 to 9;

35 R<sup>25</sup> is selected from hydrogen, alkyl, aralkyl, heterocyclalkyl, alkoxyalkylene, aryloxyalkylene, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkylene, arylcarbonylalkylene, and heterocyclcarbonylaminoalkylene; and

40 R<sup>26</sup> is selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkylene, aralkyl, alkoxycarbonylalkylene, and alkylaminoalkyl; and

R<sup>27</sup> is selected from alkyl, cycloalkyl, alkynyl, aryl, heterocycl, aralkyl, cycloalkylalkylene, 45 cycloalkenylalkylene, cycloalkylarylene, cycloalkylcycloalkyl, heterocyclalkylene, alkylarylene, alkylaralkyl, aralkylarylene, alkylheterocycl, alkylheterocyclalkylene, alkylheterocyclarylene, aralkylheterocycl, alkoxyalkylene, alkoxyarylene, 50 alkoxyaralkyl, alkoxyheterocycl, alkoxyalkoxyarylene, aryloxyarylene, aralkoxyarylene, alkoxyheterocyclalkylene, aryloxyalkoxyarylene, alkoxycarbonylalkylene, alkoxycarbonylheterocycl, alkoxycarbonylheterocyclcarbonylalkylene, aminoalkyl, 55 alkylaminoalkylene, arylaminocarbonylalkylene, alkoxyarylaminocarbonylalkylene, aminocarbonylalkylene, arylaminocarbonylalkylene, alkylaminocarbonylalkylene, arylcarbonylalkylene, alkoxycarbonylarylene, aryloxycarbonylarylene, alkylaryloxycarbonylarylene, 60 arylcarbonylarylene, alkylarylcarbonylarylene, alkoxycarbonylheterocyclarylene, alkoxycarbonylalkoxylarylene, heterocyclcarbonylalkylarylene, alkylthioalkylene,

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cycloalkylthioalkylene, alkylthioarylene,  
65 aralkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, arylsulfonylaminoalkylene,  
alkylsulfonylarylene, and alkylaminosulfonylarylene;  
wherein said alkyl, cycloalkyl, aryl, heterocyclyl,  
aralkyl, heterocyclylalkylene, alkylheterocyclylarylene,  
70 alkoxyarylene, aryloxyarylene, arylaminocarbonylalkylene,  
aryloxycarbonylarylene, arylcarbonylarylene,  
alkylthioarylene, heterocyclylthioarylene,  
arylthioalkylarylene, and alkylsulfonylarylene groups  
may be optionally substituted with one or more radicals  
75 independently selected from alkyl, halo, haloalkyl,  
alkoxy, keto, amino, nitro, and cyano; or

$R^{27}$  is  $-\text{CHR}^{28}\text{R}^{29}$  wherein  $R^{28}$  is alkoxycarbonyl, and  $R^{29}$   
is selected from aralkyl, aralkoxyalkylene,  
heterocyclylalkylene, alkylheterocyclylalkylene,  
80 alkoxyalkylalkylene, alkylthioalkylene, and  
aralkylthioalkylene; wherein said aralkyl and  
heterocyclyl groups may be optionally substituted with  
one or more radicals independently selected from alkyl  
and nitro; or

85  $R^{26}$  and  $R^{27}$  together with the nitrogen atom to which  
they are attached form a heterocycle, wherein said  
heterocycle is optionally substituted with one or more  
radicals independently selected from alkyl, aryl,  
heterocyclyl, heterocyclylalkylene,  
90 alkylheterocyclylalkylene, aryloxyalkylene,  
alkoxyarylene, alkylaryloxyalkylene, alkylcarbonyl,  
alkoxycarbonyl, aralkoxycarbonyl, alkylamino and  
alkoxycarbonylamino; wherein said aryl,  
heterocyclylalkylene and aryloxyalkylene radicals may be  
95 optionally substituted with one or more radicals  
independently selected from halogen, alkyl and alkoxy;  
and

$R^2$  is selected from mercapto,  
aryl(hydroxyalkyl)amino, N-alkyl-N-alkynyl-amino,

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- 100 aminocarbonylalkylene, alkylcarbonylaminoalkylene,  
 aminoalkylcarbonylaminoalkylene,  
 alkylaminoalkylcarbonylamino, aminoalkylthio,  
 alkylaminocarbonylalkylthio,  
 alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio,  
 105 alkenylthio, alkynylthio, carboxyalkylthio,  
 alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl,  
 alkoxyalkyl, alkoxyalkylthio, alkoxycarbonylalkylamino,  
 alkoxycarbonylaminoalkylene, alkoxycarbonylaminoalkoxy,  
 aralkylthio, heterocyclylalkylthio, aminoalkoxy,  
 110 cyanoalkoxy, carboxyalkoxy, aryloxy, aralkoxy,  
 alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; or  
 $R^2$  is  $R^{200}$ -heterocyclyl- $R^{201}$ ,  $R^{200}$ -aryl- $R^{201}$ , or  $R^{200}$ -  
 cycloalkyl- $R^{201}$  wherein:  
 $R^{200}$  is selected from:
- 115 -  $(CR^{202}R^{203})_y-$ ;  
 -  $C(O)-$ ;  
 -  $C(O)-(CH_2)_y-$ ;  
 -  $C(O)-O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-C(O)-$ ;  
 120 -  $O-(CH_2)_y-C(O)-$ ;  
 -  $NR^{202}-$ ;  
 -  $NR^{202}-(CH_2)_y-$ ;  
 -  $(CH_2)_y-NR^{202}-$ ;  
 -  $(CH_2)_y-NR^{202}-(CH_2)_z-$ ;  
 125 -  $(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$ ;  
 -  $(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-$ ;  
 -  $(CR^{202}R^{203})_y-S(O)_x-$ ;  
 130 -  $S(O)_x-(CR^{202}R^{203})_y-O-$ ;  
 -  $S(O)_x-(CR^{202}R^{203})_y-C(O)-$ ;  
 -  $O-(CH_2)_y-$ ;  
 -  $(CH_2)_y-O-$ ;  
 -  $S-$ ; and  
 135 -  $O-$ ;

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or  $R^{200}$  represents a bond;

$R^{201}$  represents one or more radicals selected from the group consisting of hydroxy, hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkylene, alkoxyarylene, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclalkylcarbonyl, alkylsulfonylalkylene, aminoalkyl, aralkylamino, alkylaminoalkylene, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkylene, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxy carbonylamino, alkoxyalkylcarbonylamino, alkoxy carbonylaminoalkylene, alkylimidocarbonyl, amidino, alkylamidino, aralkylamidino, guanidino, guanidinoalkylene, and alkylsulfonylamino; and

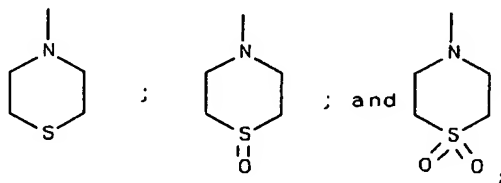
$R^{202}$  and  $R^{203}$  are independently selected from hydrido, alkyl, aryl and aralkyl; and

y and z are independently 0, 1, 2, 3, 4, 5 or 6 wherein y + z is less than or equal to 6; and x is 0, 1 or 2; or

$R^2$  is  $-NHCR^{204}R^{205}$  wherein  $R^{204}$  is alkylaminoalkylene, and  $R^{205}$  is aryl; or

$R^2$  is  $-C(NR^{206})R^{207}$  wherein  $R^{206}$  is selected from hydrogen and hydroxy, and  $R^{207}$  is selected from alkyl, aryl and aralkyl; and

$R^3$  is selected from pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

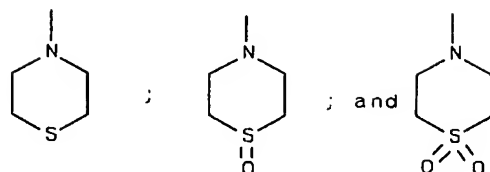


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wherein the  $R^3$  pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl,

1208

thiazolylalkyl, thiazolylamino,



170

groups may be optionally substituted with one or more radicals independently selected from halo, keto, alkyl, aralkyl, aralkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, alkylsulfonyl, arylsulfonyl, aralkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkylene, alkenoxyalkylene, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclylloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyaralkylamino, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, aralkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, aralkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, haloalkylsulfonyl, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and  $-NR^{44}R^{45}$  wherein  $R^{44}$  is alkylcarbonyl or amino, and  $R^{45}$  is alkyl or aralkyl; and

$R^4$  is selected from hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein  $R^4$  is optionally substituted with one or more radicals independently selected from halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio,

200

1209

alkylthioalkylene, arylthioalkylene, alkylsulfinyl,  
alkylsulfinylalkylene, arylsulfinylalkylene,  
alkylsulfonyl, alkylsulfonylalkylene,  
205 arylsulfonylalkylene, alkoxy, aryloxy, aralkoxy,  
aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,  
alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano,  
nitro, alkylamino, arylamino, alkylaminoalkylene,  
arylaminoalkylene, aminoalkylamino, and hydroxy; or  
210 a pharmaceutically-acceptable salt or tautomer  
thereof,

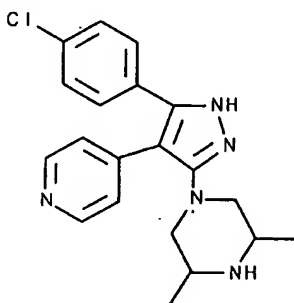
said method comprising the steps of treating a  
substituted ketone with an acyl hydrazide to give the  
pyrazole.

142. The process of Claim 141 wherein the process is  
carried out in an acidic solvent.

143. The process of Claim 141 wherein the acidic  
solvent is acetic acid.

144. The process of Claim 141 wherein the acidic  
solvent is an organic solvent containing an acid.

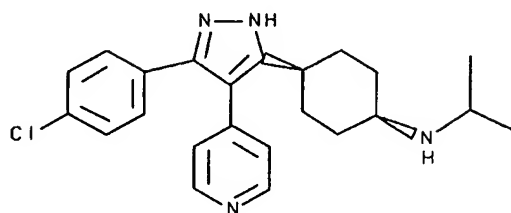
145. The compound:



or a tautomer or pharmaceutically acceptable salt thereof.

1210

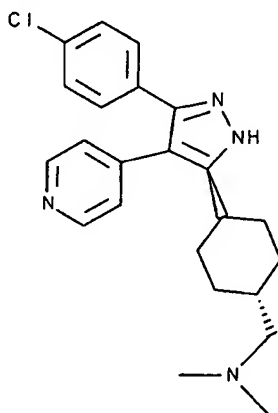
146. A compound of Claim 71 that is:



5

or a tautomer or pharmaceutically acceptable salt thereof.

147. A compound of Claim 39 that is:

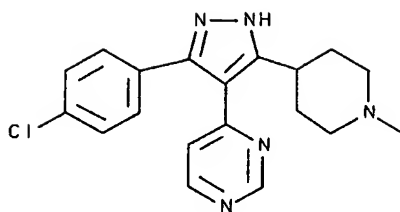


10

or a tautomer or pharmaceutically acceptable salt thereof.

148. The compound:

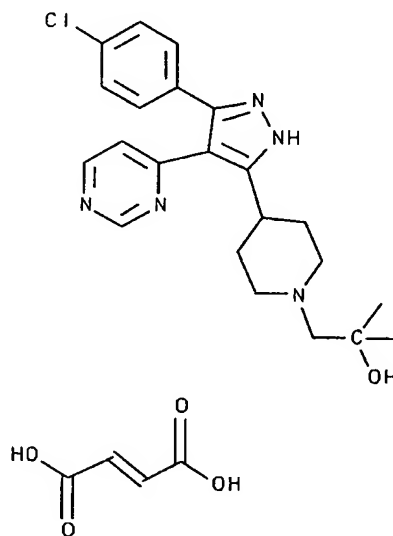
1211



15

or a tautomer or pharmaceutically acceptable salt thereof.

149. A compound of Claim 1 that is:



20

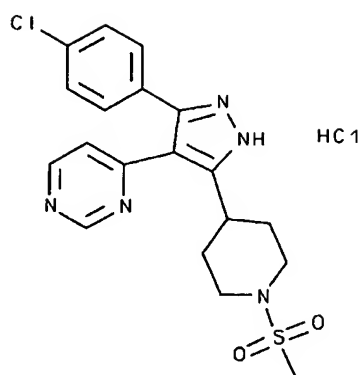
or a tautomer or pharmaceutically acceptable salt thereof.

25

150. The compound:



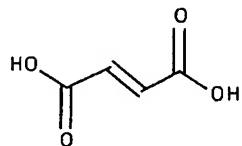
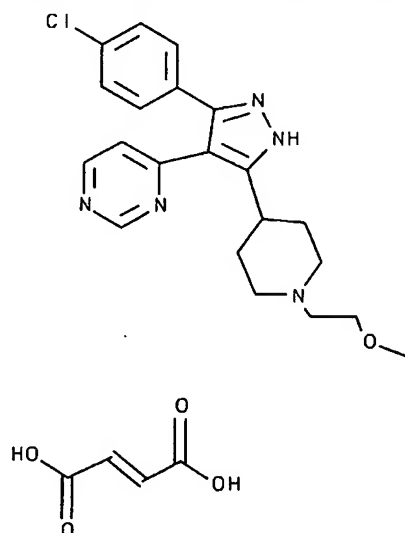
1212



or a tautomer or pharmaceutically acceptable salt thereof.

30

151. A compound of Claim 1 that is:

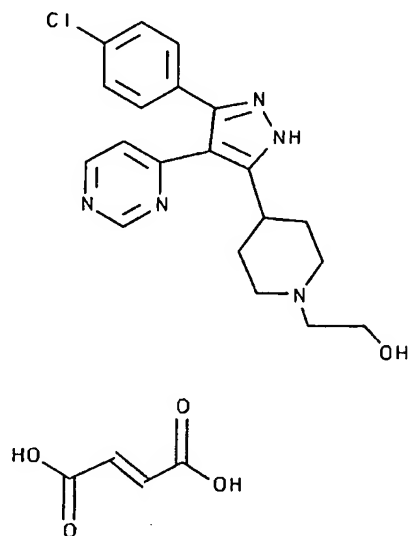


1213

or a tautomer or pharmaceutically acceptable salt thereof.

35

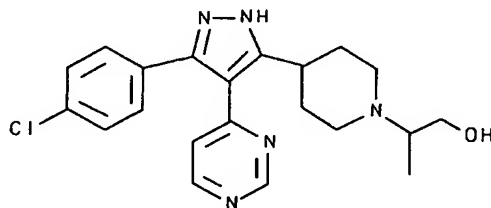
152. A compound of Claim 1 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

40

153. A compound of Claim 1 that is:

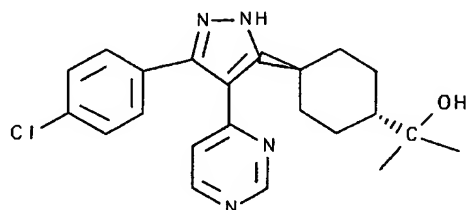


1214

or a tautomer or pharmaceutically acceptable salt thereof.

45

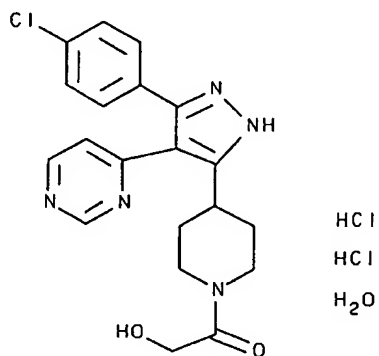
154. A compound of Claim 39 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

50

155. A compound of Claim 1 that is:

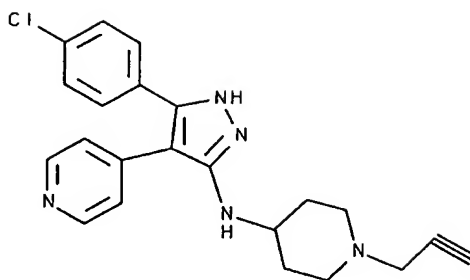


or a tautomer or pharmaceutically acceptable salt thereof.

55

156. A compound of Claim 82 that is:

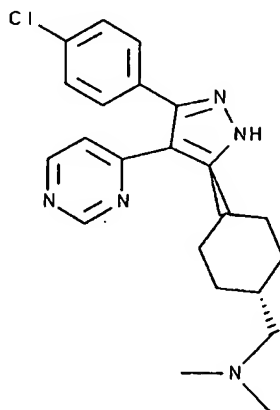
1215



or a tautomer or pharmaceutically acceptable salt thereof.

60

157. A compound of Claim 42 that is:

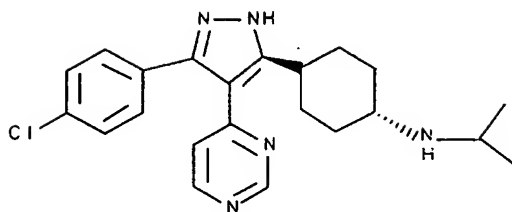


or a tautomer or pharmaceutically acceptable salt thereof.

65

158. A compound of Claim 71 that is:

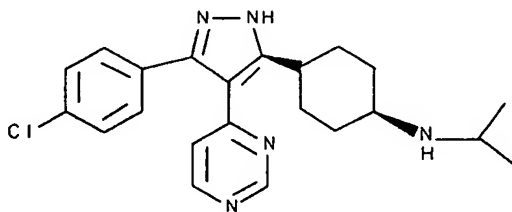
1216



or a tautomer or pharmaceutically acceptable salt thereof.

70

159. A compound of Claim 71 that is:



or a tautomer or pharmaceutically acceptable salt thereof.

75

160. A compound of Claim 70 wherein R<sup>104a</sup> is meta-chloro or para-chloro.